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"PERSONALITY DISORDERS" CAUSING DIGESTIVE COMPLAINTS

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Submitted for publication January 4, 1941

The influence of the emotions on digestion is familiar to everyone, and it is common medical knowledge that the majority of patients with digestive symptoms reveal no organic gastro-intestinal lesions. It is, therefore, frequently necessary to consider the social and environmental situation and the personality of patients with digestive complaints in seeking the cause of their illness and in planning an effective method of treatment.

With these considerations in mind a study was planned with the object of investigating the frequency and character of social problems and emotional disturbances in a series of patients admitted to the Gastro-intestinal Clinic of the Johns Hopkins Hospital Dispensary. This study showed that a large proportion of the patients were suffering from emotional or mental disturbances of which the digestive complaints were a result. These disturbances have been designated as "personality disorders" because they involve the total individual and because the study of the patients usually revealed no organic lesions to account for the digestive symptoms.

The fifty patients studied constitute an unselected series, routinely sent to the clinic by the physicians serving as dispensary admitting officers, and assigned in rotation to one member of the regular clinic staff, taken as they come until fifty patients had been studied. The series is considered to represent a fair sample of patients coming to a large general dispensary for the relief of gastro-intestinal complaints. They were all the patients assigned during the period of study to Dr. Moses Paulson who cooperated generously in the study. Eleven

[1] Aided by grants from the Josiah Macy, Jr. Foundation and from the John and Mary R. Markle Foundation.

of these patients have been reported in a paper published previously in collaboration with Dr. Paulson (1).

Each patient was first studied according to the usual routine of the Gastro-intestinal Clinic, which included a general medical history and complete physical examination, supplemented by X-ray, laboratory and instrumental methods of examination of the digestive tract. By these methods the physical status of each patient was determined before the study of the patient as a person was begun. The patients were nearly always seen in the clinic in consultation with Dr. Paulson, during or at the end of their diagnostic study, so that the continuity

TABLE 1

Physical status of 50 patients with digestive complaints

"Primary" digestive disturbances		13
Demonstrable lesions	6	
(Personality disorders, 4)		
Faulty diets	4	
Alcoholism	2	
Excessive use of laxatives	1	
Arterio-sclerotic heart disease		2
(Personality disorder, 1)		
Central nervous system syphilis		2
No demonstrable physical cause of complaints		33
		50
Personality disorders without evidence of disease	33	
Personality disorders with evidence of disease	5	
	38	

of their medical care was not broken, a point of no little importance in some of the cases.

The clinic diagnosis of the fifty cases in the series is shown in Table 1. Only thirteen patients had "primary" disturbances of the digestive tract, six with organic lesions, four with symptoms caused by faulty diets, two by alcoholism and one with symptoms apparently caused by excessive use of laxatives. There were also four patients with organic disease of other systems, two of whom had arterio-sclerotic heart disease and two had syphilis of the central nervous system, one of whom was a typical paretic and was immediately transferred to the psychiatric clinic.

Of the six patients with organic disease of the digestive tract, four had recent or previous peptic ulcers, and in all of them emotional strain or personality disorders were related to their illness. This relationship was also found in one patient with organic heart disease whose digestive symptoms were evidently of psychogenic origin. These five cases will be given further consideration. The personal studies of a patient with infestation by entameba histolytica without dysentery and a patient with benign pyloric obstruction made no practical additions to their clinical studies. Interviews were helpful in understanding the situations leading to faulty diets and to the excessive use of laxatives, but added nothing of value in treatment. Personality problems were revealed in the two cases of alcoholism, but as they bore only indirectly on the digestive complaints of the patients, these cases are omitted from discussion.

There were thirty-three patients, or sixty-six per cent, in whom no organic lesion or unhygienic habits could be discovered to account for their symptoms. These patients together with the five patients having organic lesions mentioned above, constitute a series of thirty-eight patients whose personal studies are hereafter described and analysed.

This large proportion of our patients in whom personality disorders had a causal relationship to their digestive complaints is quite comparable to the findings of others. Sullivan (2) reports that "personality factors" played a part in the production of digestive symptoms in seventy per cent of 200 patients, while Stevenson (3) found that seventy-five per cent of 150 patients admitted to the gastro-intestinal division of the Cornell Clinic in New York had emotional problems. Over fifty years ago Stiller, according to Dunbar (4), stated that from sixty to seventy per cent of all patients consulting him for digestive disturbances had "nervous indigestion". It is therefore apparent that the study and treatment of so-called "nervous indigestion" is an important function of gastro-enterology, a subject that often fails to receive the attention it deserves, especially in hospital out-patient practice.

The study of the patient as a person was initiated by an interview, carried out in a small office removed from the distractions of the clinic. It was usually begun with a review and elaboration of symp-

toms, in order to establish a satisfactory doctor-patient relationship and to confirm or correct the initial history. The patient was then asked to tell about the conditions of his life that might have bearing on his symptoms, especially at the time of their onset, or as related to periods of increased severity. At this time it often seemed advisable to inform the patient of the possible relationship between emotional strain and digestive symptoms, and to review with him the results of the study of his physical status. Following these explanations a social history was usually readily obtained, including an account of personal relationships, moods, emotional tension in the home or at work, sexual problems, worries, anxieties or frustrations. An effort was made to obtain the story of each patient by the use of guiding questions, but without giving explanations, and by giving the impression of being an interested, sympathetic listener who was in no way passing judgment on the rightness or wrongness of behavior, by whom intimate revelations would be treated confidentially and used for the benefit of the patient. Evasions were looked for and the patient was often helped by further questioning or by brief explanations. The histories thus obtained revealed in a satisfactory manner various situations through which the patients had passed, and in which they were living. The amount of note-taking during the interviews varied with the patients, but all were fairly extensively recorded by dictation as soon as possible after each interview. Patients were usually interviewed two or three times, the length of the first interview averaging about forty-five minutes, while subsequent interviews were shorter. The patients were visited at home whenever practical and members of their families were interviewed in some cases. These methods threw light on the personality and environment of the patients such as is naturally available to the family physician who visits patients in their homes. As a matter of fact, our study was considered to represent a collaboration of the specialist and the family physician as far as the conditions of dispensary practice would allow the establishment of these relationships.

The record of each patient includes an abstract of his study, diagnosis and treatment in the clinic, an account of each interview and of the home visits that may have been made, a description of the personality traits of the patient that were observed and a summary

of the more important data. The majority of the patients were followed for from several weeks to a year, reports being received by letter from those who could not be visited after their discharge from the clinic. These records have been condensed for reporting, with the elimination of identifying details. These records were used not only as a means of collecting data for study, but also to preserve the continuity of interviews. The record of each interview was reviewed prior to the subsequent visit of the patient in order to recall what the patient had said and his characteristics, as well as to bring to mind points requiring further explanations or which seemed especially important to the patient.

This use of recorded interviews deserves some emphasis, as there are innumerable conversations carried on between doctors and patients regarding problems of the greatest importance to patients, which are never included in dispensary records. In consequence, the doctor may well remember at a subsequent visit what he has said to the patient, but have no record or recollection of what the patient said to him, even if the patient had been given a favorable opportunity to express himself, which is not so frequent in the usual routine of dispensary practice. This lack of recording places the patient in a dissatisfying position and diminishes the value and directness of the doctor's advice.

The method of treatment that was employed was a simple, brief form of psychotherapy which dealt largely with social situations and obvious conflicts. After the patients had described their illness, their problems and disturbances, an attempt was made to review them with the patients with an objective and unemotional attitude in order to transfer them as much as possible to a factual and reasoning level.

An effort was also made to have the patient understand the relation of his digestive disturbances to his personal difficulties, by recounting experiences with other patients, by explanations of the effects of emotions leading to impulses of "flight" or "fight," as described by Cannon (5), and in some instances by the use of helpful reading. In all instances, however, explanations, discussions and reassurance had to be fitted as closely as possible to the personality traits and situation of each patient, and with careful consideration

of his ability to comprehend his own situation and what was said to him. These procedures therefore varied from patient to patient in a way that can only be illustrated by case reports.

It was obviously necessary in the few brief interviews that were used, to endeavor to deal with the essential material that patients readily revealed, and very little could be learned of subconscious or deep-lying disturbances of personality. It is because these simple methods, practicable for any physician who will give them time and thought, achieved such good results in many of these patients, that they deserve emphasis.

The interviews and explanations were of course only one factor in the successful treatment of the patients, since the negative findings in the clinic, assurance by the doctors there, medication such as belladonna and mild sedatives, and the general effect of admission to a highly-regarded hospital were among the other beneficial factors.

All the patients with personality disorders may be considered to have a neurosis, but the majority of them suffered from what has been termed a "situational neurosis", which occurs in individuals whose personality is otherwise intact and undistorted, but who react normally or perhaps excessively to external situations which are filled with conflict. On the other hand, some of the patients apparently suffered from a "character neurosis" with the main disturbances in the deformation of the character. This distinction of the neuroses has been discussed by Horney (6). It is evident that the simple form of treatment that was used is often successful in patients with situational neuroses and unsuccessful in those with character neuroses. In the latter the causes of symptoms lie much more deeply in the personality of the patient and cannot be effectively treated by superficial methods.

It is of course difficult to determine by a few interviews to what extent a character neurosis determines the reaction of the patient to the situation he has to face. In many cases both the situation and the personality are at fault. However, the response of the patient to efforts to adjust his situation often gives a clue as to the status of the personality of the patient.

Our meagre knowledge of the personality of the patients in this series, as well as lack of experience and skill in the field of psychiatry, makes it impractical to attempt to group the patients according to the

relative importance of situational and character neuroses in each case. This concept is, however, useful in forming judgment as to the sort of treatment a patient should have and in forecasting a prognosis.

It seems practical, however, to group the patients according to the symptoms of their neuroses, based on the types of reactions they revealed. This has been done on the basis of a classification described by Billings (7), who uses the concepts of Adolf Meyer for this purpose[2]. This grouping is made on the basis of the outstanding characteristics of the reaction of the patients to their disturbing situations (Table 2).

The number of patients in each group is given in Table 2. They are subdivided into those who responded favorably to treatment and those whose response to treatment was not favorable. The patients

TABLE 2

Patients with personality disorders

	TOTAL NUMBER	RESPONSE TO TREATMENT	
		Favorable	Unfavorable
Excessive emotional reactions	15	12	3
General nervousness	4	0	4
Anxiety attacks	1	1	0
Hypochondriacal reactions	13	10	3
Hysterical reactions	3	0	3
Depressions	2	0	2
Total	38	23	15

are reported and discussed according to this grouping and their response to treatment.

Each case is described either briefly or at some length in order to demonstrate the variety and character of the personality disorders that were encountered in this fair sample of fifty gastro-intestinal patients as seen in an out-patient clinic.

CASE REPORTS

1. Patients with Excessive Emotional Reactions

The fifteen patients in this group present the purest type of situational neurosis. They were all facing social situations causing con-

[2] Dr. Thomas A. C. Rennie of the Department of Psychiatry kindly reviewed the cases and gave valuable advice regarding their grouping.

flicts of frustration, disappointment and other emotional strains over relatively long periods, which had eventuated in the production of somatic symptoms. With the exception of two patients they seemed to have intact and undisturbed personalities. Twelve of the group were relieved of their digestive complaints by the methods employed, while three did not respond favorably. The favorable cases are first reported.

Case 1. A twenty-six year old unmarried woman who gave the impression of being a well-educated, efficient office worker, came to the dispensary in a somewhat desperate mood, saying that she could scarcely carry on her work any longer and that something had to be done for her. She had had attacks of "indigestion" with occasional spells of vomiting for years, and for the past six months had felt fatigued and depressed with attacks of nausea and vomiting about four times each week. During the ten days before coming to the hospital she had had complete loss of appetite, a gagging sensation whenever she attempted to eat, and had developed persistent constipation resistant to laxatives. She had during this time several weeping spells when at work and every evening on reaching home. She said she was overwrought and depressed.

This patient lived at home with her parents, both of whom were old and disabled, and for whom she was the main source of support. She was the youngest of six children, all of whom except herself had married and left home. Her home life was uncongenial and there was a considerable amount of repressed friction there.

This young woman had been educated in a Catholic school, where she had always led her classes, was a devout member of the church, and had maintained an intimate association with the sisters who had been her teachers. She described readily her emotional status, of which she had a good insight, as consisting of strong sweeps of sexual desire that made her feel she "could conquer the world" at times and plunged her into depression at other times. She gave way to promiscuous sexual intercourse every five or six weeks, which always produced strong conflicts with her religious sentiments. She said she was unable to lead the quiet, well-ordered life she desired and knew she should lead, but was constantly disturbed by feelings of tension and sweeps of emotion. The factor that apparently precipitated her severe symptoms which brought her to the hospital, was the strain of a new job, in which she had to struggle constantly to keep up, and the strain of doing so evidently created a vicious circle with the symptoms of her illness.

The patient was evidently eager to avail herself of the opportunity to tell her story, which she did with good judgment, directness and unusual brevity, and although it contained several problems related to her situation at home and at work, it seemed clear that the conflict between her religious sentiments and sexual drive was the problem deserving primary attention. It was given careful

consideration and discussion with her at her second interview, when she was persuaded to make an effort to appeal more strongly to her religion as a substitute for her sexual drive. This idea was emphasized at a third brief interview when her symptoms were greatly improved.

Four months later this patient wrote a letter, which is quoted with her permission. "From the medical standpoint, I know you will be glad to learn that my health has improved, my old enemy, indigestion, has been subjugated, my appetite has become normal, and the work at the office has lessened somewhat. From the psychological standpoint, which really was the cause of my trouble, your treatment has proved most beneficial. At first it was difficult to adjust myself to a new mode of thinking and living. However, I remembered the advice you had given me about becoming stronger in my faith. That course opened the way to happiness and peace of mind. Naturally, my physical being reacted favorably to my emotional attitude. I would have written to you sooner, but I wished to have an opportunity to really prove to myself that I could be different, not just enthusiastic over a new idea. As you may surmise, there are still obstacles to overcome. One of them is a gnawing restlessness that makes me happy one minute and ready to cry the next."

The patient was seen casually about five months after writing this letter, when she looked happy and cheerful and said she was very well. The success of treatment in her case was largely because she had intelligence, insight and fine sentiments, which could be guided so as to direct her thoughts and behavior.

Case 2. A thirty-three year old industrial worker complained of epigastric pain, flatulence and general abdominal discomfort. His symptoms had become annoying about ten months previously, and had been distinctly worse during the past four months since one of his four children had fallen from a boat when at play and was drowned. He was evidently depressed and had gradually lost his previous enthusiasm for his work in a large steel plant, where he was well-paid for responsible skilled work with a congenial group of fellow workmen. At the time of admission his symptoms had brought him to the point of giving up his work. The patient was somewhat restless, had a tense, anxious expression and appeared to be "high-strung".

The patient had an absorbing form of recreation in hunting and shooting, being devoted to his dogs and guns with which he spent many week-ends. He defined his childhood as "rotten", as he was one of seven children with a "lazy", hard-drinking father and grew up in an isolated mountain community in Western Maryland, where his love of hunting was developed.

Inquiry as to family relations brought out a story of constant friction between him, several brothers and members of his wife's family. He was the only member of a large family group who had a good work record and economic security. Some of his numerous nephews and nieces were constantly at his home at meal time to be fed, and he had loaned money, a shot-gun, an automobile and other things to

members of both families, and nothing had ever been returned. He had attempted to move away from his relatives, but to no avail, for they always followed into the same neighborhood, and he was constantly angry whenever his brothers or members of his wife's family were about, as he disapproved of them heartily and was annoyed because they showed a lack of confidence in him when he tried to advise them.

The story of family friction was confirmed by the patient's wife, and it was made clear to her and to the patient that his illness was caused by emotional strain, since the physical examinations had revealed no cause for his symptoms. The patient was advised to change his attitude toward his relatives, and his wife was told to protect him from family friction as far as possible and to remember that if this could be done he would get well. She was understanding and cooperative, and by their working together the patient was almost immediately relieved. When visited at home six weeks later he said he was letting his worries roll off "like water off a duck's back", and that his symptoms had almost completely disappeared. He was in excellent spirits, and appeared to have a change of temperament, especially when exhibiting his set of fine guns. He remarked that he had learned a lot about not worrying and was no longer disturbed by his family relations, as he had refused to become involved in them. When seen six months later, he reported a gain of twelve pounds, appeared quite jolly and was delighted with his recovery, and although he had indigestion now and then, it no longer bothered him.

Case 3. A thirty-one year old Polish house-wife complained of epigastric pain and soreness along the costal margins, which had been fairly constant for two years. She had lost weight and was constantly fatigued, and was overcome frequently by weeping spells which could be controlled only by the assistance of her mother's comforting. She had developed a fear of tuberculosis. Examinations in several clinics failed to reveal any physical cause for her symptoms.

The patient was an attractive, rather alert, apparently cheerful young woman. She had come to this country from Poland at the age of eighteen, found employment without difficulty and in less than three years had married a Portuguese machinist. Soon thereafter, about ten years ago, she brought her mother and father from Poland, and they had been supported by her husband as members of the household ever since. Her father was a cabinet-maker by trade, but had been almost constantly unemployed. In spite of the fact that he and his wife were being supported by their son-in-law, the father attempted to dominate the family, constantly criticizing the patient's husband from whom he differed markedly in racial characteristics, age and temperament.

The patient's symptoms began when the family group which included two small daughters, was further complicated by the temporary inclusion of an unemployed brother-in-law, who seemed rather worthless to the patient and annoyed her, but it was the friction between her father and husband which she thought

was the main cause of tension in the home. After reviewing the situation with the patient and pointing out the probable relationship of the friction at home with her illness, she was told to come again with her husband.

Her husband was an attractive man of characteristic Latin traits, and strikingly different from his wife in appearance and temperament, but appeared alert, clever and industrious. He had a responsible job as a machinist. He said he was constantly telling his wife not to worry, and was evidently annoyed by her illness. After the nature of his wife's illness was explained to him in her presence, they were both advised to take a more indulgent and less serious attitude toward the old father. The patient was advised to laugh instead of cry at the differences between her father and husband, and as she seemed to have a quick sense of humor, she thought she could do so. A week later she said the situation at home had changed definitely and she was greatly relieved, both in mind and body. Nine months later she reported in person that her home life was very satisfactory, and that she was perfectly well.

Case 4. An unmarried woman of fifty-six had suffered from the usual symptoms of indigestion for about ten years, ever since her mother had died and left her as the only survivor of a large family. Her symptoms had gradually become worse and more constant as her economic situation had become gradually more insecure, and she thought her symptoms were related to financial worry. She gave the impression of being an anxious spinster who was endeavoring unsuccessfully to maintain a former social level. Her story contained evidence of frustration and disappointment, and she appeared unstable and fearful. She said she had undergone treatment for seven months in a psychiatric hospital at the age of twenty-five. The details of this illness could not be ascertained.

The only financial asset which this patient possessed was a rather large house which she had inherited, and which had lost much of its value, both as real estate and as a rooming house, since its neighborhood had been taken over by colored people. She was the only white resident left in her block and she could rent her rooms only to tenants of low quality, who frequently failed to pay their rent, as she was relatively powerless to force them to pay.

The patient was advised to accept assistance from friends and to sell her house. She was given encouragement and backing in carrying out plans which would relieve her state of worry and uncertainty. In two months these plans were well formulated by her own efforts, and her digestive symptoms which had annoyed her for years had, she claimed, entirely disappeared.

Case 5. A twenty-seven year old Italian tailor, who presented evidence of emotional instability as a racial rather than as an abnormal individual characteristic, was disturbed because he thought his abdominal pain of rather brief duration was caused by appendicitis, as had been suggested by a physician. He was under considerable emotional strain because his work had shut down and he was

being supported by his wife. His adolescence had been filled with difficulties and had apparently increased his natural instability and anxiety. Two days after he was told of his negative physical examination and of the relationship of abdominal pain and emotional strain, his symptoms had entirely disappeared.

Case 6. A twenty-nine year old divorced woman, with an adolescent daughter, had had indigestion, nervousness and a singing noise in her head for nine months. She had had severe insomnia for two months, frequent crying spells and much discomfort after eating. She said that she had repressed the outward manifestations of her disturbances as far as she could for the sake of her daughter, but had developed a fear of tuberculosis. This patient appeared to be rather deeply depressed, and had reacted excessively to her social problems. It was surprising to find how readily she responded to an explanation of her symptoms and to advice regarding the relation of her illness to her emotional disturbance, as her symptoms had practically disappeared in a week, and she remained perfectly well up to the time she was last seen two months later, when she gave the impression that she would remain well.

Case 7. A forty-five year old house-wife had had headaches, fatigue and "nervousness" for several years, which she attributed to her menopause. In addition to these symptoms she had developed during the past three months loss of appetite, almost continuous nausea, daily weeping spells and a desire to be alone. She was much disturbed by her five children of school age, and described a considerable degree of tension in her home life of which she was the center, but caused by no definite social problem or marital friction.

The patient was a rather obese, sturdy woman who seemed anxious, suspicious and at first quite reticent, but as the interview progressed she talked freely, and later brought her husband for an interview. He appeared to be a rather anxious, impatient man, disturbed by lack of work as a master plumber and somewhat annoyed by his wife's illness. The husband, the care of her five children and probably menopausal disturbances had created a situation to which this patient reacted excessively.

It was explained to the patient and to her husband that she had no organic disease and that her symptoms were caused by emotional strain. An attempt was made to persuade her to think rationally about her daily problems, rather than to react emotionally to them, and to break her mentally unhygienic habits. This she succeeded in doing, as when visited at home four months later she appeared cheerful, said she was quite well and evidently had her emotions under much better control.

Case 8. A forty-eight year old housewife had been worried and emotionally disturbed for nearly a year, and had developed during this time abdominal pain, discomfort and flatulence, for which she sought relief. One of her sons had been

found to have syphilis, and she came to the hospital on request for an examination, when her Wassermann reaction was found to be positive and she was told she required treatment. She had no other evidence of syphilis. Her son's infection was considered to be congenital and there was inconclusive evidence that her husband was the source of infection. The patient was a home-loving, church-going, steady type of housewife, who seemed to be a normal, well-integrated and satisfied person. However, she said she was "worried to death" by the thought of syphilis in the family, which had "gotten on her nerves." Her digestive symptoms soon disappeared after she had an opportunity to have a discussion of the situation and was given a better understanding in regard to the nature of the disease and its prognosis under treatment.

This case is of interest as an example of the emotional strain that may accompany a diagnosis of syphilis, and of the disturbing problems that it may create in a family situation.

Case 9. A twenty-one year old Polish housewife was pregnant for the third time, and had abdominal pain and distress which had been present for two years.

She was depressed and discouraged, and was anxious to be given contraceptive advice. There had been much disappointment and friction in her married life, and she had rather strong resentment toward her husband because of his neglect and alcoholic excesses since the birth of her last child. An effort was made to relate her emotional reactions to her digestive symptoms, and to persuade her to change her attitude toward her husband so that she would be less disturbed by his behavior. After the delivery, contraceptive advice was given to her in the Maternal Health Clinic. Three months later she said she was free from the digestive symptoms that had brought her to the clinic.

The last three cases in this group of favorable cases had organic disease. Two of them with peptic ulcers were much benefited by ulcer treatment, one of them requiring a surgical operation for a hemorrhage. These patients are included in this group because in both cases a personality disorder seemed to be a precipitating cause of their illness, while little or no credit can be given to psychotherapy, especially in the first case.

Case 10. A fifty-eight year old school janitor from West Virginia complained of digestive symptoms for two years, and when found to have a gastric ulcer was admitted to the medical ward. An operation was required for a hemorrhage while in the hospital. His symptoms had developed after he had lost his position as a mill-right, and he had been without steady employment for five years.

He had divorced his wife when forty years old, because she was extravagant and got him into debt. He had contemplated divorce for seven years before taking action, as he said he "drifts a long time before he acts". He revealed

much concern over money matters, evidently put much store on the possession of money, and was excessively disturbed by his previous economic insecurity. He gave the impression of being unstable, emotional and fearful, and his symptoms developed when under the strain of economic insecurity.

The patient made a good recovery, and wrote six months after leaving the hospital that he was getting on very well, with strict attention to his diet.

Case 11. A forty-nine year old housewife was admitted to the hospital because of a hemorrhage from a duodenal ulcer, and was referred to the dispensary at the completion of her apparently successful treatment in the medical ward. She seemed well integrated and emotionally well controlled. Her story revealed a life filled with difficulties including marital friction and numerous problems involved in the rearing and behavior of her six children. The onset of her digestive symptoms followed refusal of her husband to have her old father in the household, and her father's death soon after his enforced removal from the home. Her gastric hemorrhage had occurred after one of her sons had married and brought home a fifteen year old wife. She was obliged to care for the wife and her one month old baby, and during this time she developed apparently unreasonable anxiety regarding her sixteen year old daughter, a constant sense of fatigue and a desire to be alone. Her childhood had been disturbed, and her mother had been twice divorced.

The patient responded well to a discussion of her problems, and advice was given to her in regard to her emotional reactions in relation to her illness, which she accepted gratefully, and which seemed essential for the successful treatment of her duodenal ulcer. The future course of this case was not learned.

Case 12. The last patient in this group was a fifty-nine year old unemployed baker, who complained of chronic constipation. He was found to have arteriosclerotic heart disease, with auricular fibrillation and a mild pernicious anemia, readily controlled by liver therapy. His constipation had begun two years previously when he lost his job, and he was depressed and anxious because his savings were being used up and he feared destitution. He was also disturbed by a son to whom he had loaned money and from whom he could get no adequate response. A discussion of his affairs and the suggestion of a plan which seemed practicable to him, together with rational use of laxatives, improved habits and digitalis, were factors in producing a much more cheerful, brighter and more comfortable condition of body and mind. He said that his only regret was that he had not come sooner to the hospital.

This case is worthy of emphasis as an example of an emotional disturbance in a patient with organic disease, creating a situation in which personality difficulties are so often overlooked, but which are in reality of basic importance in successful medical care.

There were three patients in this group of fifteen whose symptoms were not relieved, all of whom presented situations which could not be adjusted.

Case 13. A thirty-five year old married woman complained of increasing abdominal pain and discomfort, flatulence, constipation and fatigue, especially in the morning hours. These symptoms had been present for three years. She was depressed, discouraged and wept while being interviewed. Her tubes and ovaries had been removed eight years previously when twenty-seven, and the operation had been followed by peritonitis. Her appendix had been removed five years later, and more recently doctors had told her she had abdominal adhesions which would eventually require another operation, that her blood-pressure was low, and that she might have gall-stone disease. She had also developed a fear of cancer. Examinations in the Gastro-intestinal Clinic revealed no evidence of organic disease.

The patient was well educated, intelligent, attractive, and had good insight into her complicated problems. She had married, at the age of twenty-one, an older man with whom she was not in love, and had a thirteen year old daughter, her only child, on whom her love was centered, and for whom she had frustrated ambitions. Her respect for her husband had broken down during the past ten years, while he was out of employment most of the time, not making serious attempts to find employment and being supported by the patient, who had a position in a government bureau. Her feelings toward her husband were turned to antagonism when she found that he had loaned without her knowledge some of her savings to an unreliable relative. It was after this discovery that her symptoms became worse. The care given by her husband to her child, which allowed her to continue with her work, stood in the way of a separation, and may also have been a cause of jealousy which she did not admit. Her work was of a repetitious routine type which allowed opportunity for worry and self-pity, although it was not uncongenial. Christian Science lectures and books dealing with psychological adjustment had failed to give her relief, although she had struggled to get it.

This patient presented a situation which seemed impossible to alter, especially since she lived away from Baltimore and it was impracticable to discuss her situation with her husband. After several interviews she said that she had gained a better understanding of her illness and its causes and this understanding had definitely benefited her. She was encouraged to carry out her plan for a "rest cure", and some weeks later wrote an appreciative letter in which she said that "if I find health and happiness in the future, I intend to write you of it." However, nothing further was heard from this patient. Her severe digestive complaints were coincident with a prolonged state of tension brought about by dissatisfying marital relations, complicated by a deep attachment to a child.

Case 14. A forty-nine year old unemployed electrician complained of almost constant abdominal discomfort and indigestion, which had been present for nine months. He was a large, well-built, heavy-set man, who was somewhat overweight and who gave the impression of having a rather jovial, somewhat inadequate personality. He appeared anxious, tense and frustrated, and said that before his marriage at the age of thirty-five he had been a "happy-go-lucky", socially inclined and generous fellow, but had become gradually discouraged by failures and worried because he "gets all the tough breaks". His family consisted of his wife and two children of school age.

The patient had had a somewhat varied and unsuccessful career, which included work as an electrician, graduation from a law school, unsuccessful law practice, service on the police force and a short period of employment in his father-in-law's manufacturing plant. He had married into a well-to-do family, who had been called upon to support his family. Marital friction had begun about ten years previously after the birth of his second child who was unwanted by his wife. He felt obliged to take her complaints and nagging with much repression of feeling, because of his dependence, but had occasional outbursts of temper. He described much emotional strain in the home-life, for which he had no adequate outlet, and which he said made his life miserable. No other cause for his digestive disturbances was revealed.

The patient would not consent to a home visit, and doubtless failed to disclose some of the disturbing elements in his life, but he gained some understanding regarding the nature of his illness. However, he reported three months later that he continued to have some digestive complaints, and that he had been unable to obtain satisfactory employment, as he was advised to do. He then said that his nagging wife was the only serious problem he had to face, but it seemed impossible for him to solve this problem by his own efforts.

The other patient in this group of unfavorable cases lacked sufficient intelligence to understand his problems.

Case 15. A twenty-two year old, boyish-looking man complains of abdominal discomfort and constipation, for which he had taken many laxative drugs. He had been nervous, with choking sensations and indigestion, ever since an automobile accident four years previously in which he was not injured, but he had been "sickly" all his life. He was distinctly undersize, and apparently mentally retarded, for he had never learned to read or write. He was one of six children, who with their parents, travelled around the country making and peddling artificial paper flowers, living in an automobile trailer or tent, and were members of a gypsy-like Irish clan. It seemed evident from his story that the patient's symptoms had been precipitated by a shocking episode and had been sustained by an unhealthy life in which he was unable to maintain himself on an equality with his brothers, and was under constant strain in his efforts to do so. Doubtless, his

lack of insight and mental retardation were in some measure responsible for his complaints. He gave no definite evidence of improvement on subsequent visits.

Of these three patients whose treatment was not definitely beneficial, two had emotional disturbances caused primarily by marital friction which could not be lessened, and to which the patients could not be adjusted. The chief difficulty lay superficially at least in the social situation to which the patients reacted, although in the second case, number 14, the patient seemed to lack average ability to work out his problems effectively. The third case was unmodifiable human material, with an intelligence level of a moron.

All the patients suffering from situationally determined reactions, except the last one, were entirely conscious of their problems, had ruminated over them for a considerable length of time and accepted readily the relationship of their personal difficulties and their digestive complaints.

2. Patients with General Nervousness

There were four patients who presented what seemed to be an inherent quality designated by the vague term general nervousness. They were judged to be inadequate in meeting their problems of existence, and their digestive symptoms were more or less passing episodes in unsuccessful lives. Two of these patients were relieved of symptoms, at least temporarily, but as no lasting benefits were to be expected from the type of treatment being employed, no persistence of effort was used.

Case 16. A twenty-six year old colored man complained of abdominal pain extending into his scrotum. He was living a hand-to-mouth existence, and his diet was probably improper and irregular. He was a nervous, restless person, a rather unusual type among the negroes. He said he had been "nervous and shaky" all his life, but especially so for the past five years, when his mother died suddenly, followed in four months by the death of his father, who was shot at a picnic and died in the patient's presence. He had seen the ghosts of his parents on three occasions, and on one of these occasions he had screamed loudly and was much shaken by the episode.

The patient was unusually disturbed by his mild digestive symptoms, and seemed much relieved by an opportunity to discuss his experiences and his symptoms. As he did not return to the dispensary, it was thought that the apparently exaggerated discomfort of this patient had been relieved.

Case 17. A thirty-five year old colored woman was referred to the gastro-intestinal clinic from the psychiatric clinic, because of digestive symptoms and a choking sensation. She had recently been a patient for six months in a psychiatric hospital, and said that her mother was then in a city hospital for "nervous trouble". Her maternal grandmother, aunt and uncle had all died in a state psychiatric hospital and one of her children was to be admitted to the state school for feeble-minded children as soon as a vacancy occurred.

This patient was the only one in this series who had not been admitted directly to the gastro-intestinal clinic. Her mentality was of a low grade and no physical abnormalities were found. Her digestive symptoms soon disappeared after medicine had been prescribed, and after she had been encouraged to give less attention to her digestive tract.

Case 18. A forty year old Jewish housewife complained of gastric pain, especially marked when fatigued, which had begun four years previously when she was much worried because of financial difficulties and economic insecurity, exaggerated by a uterine hemorrhage and by an injury to her hand. She came to the hospital because she feared she was seriously ill, and was relieved by her negative examinations. The interview revealed no serious adverse social conditions, but it was clear that the patient was unstable, tense and introspective, and that her excessive reactions were largely responsible for her symptoms. She did not wish to go into her personal affairs, so the interview was brief and incomplete.

Case 19. A forty-four year old Russian Jewish tailor had suffered from indigestion since the age of ten, and said that his symptoms were similar to those of his mother. His digestive symptoms had been constant for about twenty years, and ten years previous to his present admission a diagnosis of duodenal ulcer had been made in the hospital. He had returned to the dispensary because his abdominal symptoms had become exaggerated four months previously when his piece-work employment had become so scant that he was unable to support his family adequately and could not obtain proper diet for himself. This situation had added new worries to those he had carried throughout his life, and his symptoms were referable to a spastic pylorus. The patient was emotionally unstable, anxious and fearful, and these qualities were considered as personality characteristics conditioning his reaction to his economic problem. Three months later, he was no better than when admitted to the clinic.

3. A Patient with Anxiety Attacks

Anxiety attacks are characterized by the more or less sudden onset of the physiological manifestations of fear or anxiety, such as difficulty in breathing, choking sensations, palpitation, sweating and weakness accompanied by a sense of apprehension as of impending death. There was only one patient who presented this picture.

Case 20. A twenty year old married baker began to have digestive symptoms at the time of his marriage, seventeen months previously. These symptoms gradually increased in severity and had for five or six months before admission taken the form of attacks coming on usually when he attempted to eat. He said he would be seized suddenly with a severe choking sensation, difficulty in breathing and cardiac palpitation, which would force him to rush from the room he was in with a fear that he would die. His physical examinations failed to reveal any evidence of disease, and although the interview brought out the fact that he had married without the approval of his wife's family, and was unpopular with his mother-in-law, he gave the impression of being undisturbed by this situation. He related the early episodes of his life with cheerfulness and with a show of humor, telling with apparent pleasure of his school life and his success as a saxophone player at high school and with a professional group.

Then, with hesitation and effort, the patient said in a different tone, that his real trouble was a constant fear of tuberculosis, and proceeded to give his reasons for this fear. During his boyhood, his next-door neighbor had been a boy seven years his senior, whom he had always admired for his athletic ability and for other traits he hoped to acquire. About six years before, this friend had married at the age of twenty-one, and soon thereafter was found to have tuberculosis. From that time on the patient had seen his friend's health gradually fail, and had often sat with him to keep him company. Six months after his neighbor's wife had had a baby, his neighbor had died. From that time on the fear of tuberculosis had been on the patient's mind, stimulated by his mother's warning that he might have contracted the disease, and would probably die of it if he did not stop playing the saxophone and sitting up late. This fear had increased at the time of his marriage, when his symptoms began, becoming more marked during the course of his wife's pregnancy. He said that their baby was expected within a few weeks. Since his mother had even suggested that his wife might have tuberculosis, he was thoroughly frightened. It was clear why his symptoms had begun at the time of his marriage and were aggravated by his wife's pregnancy, as his fate, he thought, was to be quite similar to that of his friend. He said that if he could get the worry regarding tuberculosis out of his mind he thought he would be "one hundred per cent better".

The patient responded well to the statement that none of his symptoms suggested tuberculosis, and that his examination revealed no evidence of the disease. It was explained to him that his fears were natural, and that his symptoms were characteristic of anxiety. He was told to go home and tell his mother, with whom he lived, that he had never had tuberculosis. He returned in two weeks to say that all his symptoms had disappeared, that he wanted to return to work, and that he could eat with comfort. A visit to his home was made a few days later, when he was found to be elated over the birth of a son the day before. An opportunity was found to impress upon his mother that she was never to mention tuberculosis again to her son.

This case is impressive as an example of the value of the interview as a means

of determining the true nature of an illness, as revealing its underlying cause and the type of treatment needed. The patient was a rather sensitive, reticent young man, who did not readily admit anxiety, and it seemed doubtful if assurance regarding his digestive symptoms alone would have given him relief.

4. Patients with Hypochondriacal Reactions

Patients with hypochondriacal reactions are those whose thought and attention become centered on their bodies, in this series especially upon their digestive tracts, although some of them had a fear of a disease that should have produced symptoms elsewhere. Such patients frequently have a sense of insecurity, fall an easy prey to injudicious medical advice from the laity or from doctors. Their symptoms are usually localized and they are not as generally disturbed as the patients in the foregoing groups.

There were thirteen patients who belong in this group, ten of whom responded favorably to treatment and three who did not. The favorable cases are the following.

Case 21. A robust, cheerful-looking colored housewife of thirty-five complained of epigastric pain over a period of three years, for about two years intermittent, but constant for a year. No organic cause for her pain could be found and in her first brief interview she said she had no worries and that she had a peaceful life in the country as a farm worker's wife without children, but interested in her vegetable garden and in raising chickens. At the second interview, however, she admitted that she had a constant fear of death from cancer of which she felt so sure that she had made all her funeral arrangements before coming to the hospital. Her symptoms had begun after listening to a radio talk on cancer in which the early symptoms of cancer of the stomach had been described. Since that time, over a period of three years, she had always listened to the weekly health talks and had read all she could find regarding health in newspapers.

After the true status of her physical condition had been explained to her, and after the relationship of her anxiety and her symptoms had been discussed, her epigastric pain soon disappeared. In three weeks she reported that she had been without pain for nine days and that she was greatly relieved by lack of worry. She gave some of the credit to the medicine, belladonna and phenobarbital, that had been prescribed, and said that after having been in "great misery" for three years, she felt quite well. Three months later she wrote that she was without digestive symptoms, although she was very nervous at times, but that the interview had changed her outlook regarding her health, over which she no longer worried.

Case 22. A twenty-six year old salesman said that for eight years he had had diarrhoea with five or six loose, watery bowel movements a day. Recently, this

ailment had become especially disturbing, as he was obliged to have a bowel movement after every meal, and it had become an increasing source of anxiety, interfering both with his efforts to make a living and with his courtship of a young lady whom he hoped to marry.

The patient was an intelligent, emotionally unstable young man, who talked fluently and with slight excitement, and who had done well in high school and in a business college. He recalled the day and the circumstances when his diarrhoea had begun at the age of eighteen, a few days after losing his first job, and that it had been constant since that day. As he had been unable to find another job, he had spent six years helping his father who had a small tailoring business and who did not really need him. His life at this time was constantly unsatisfactory. He had developed a fear of appendicitis, but had been afraid to consult a doctor because an operation might be advised. He had developed a habit of erotic fantasies and masturbation which he could not control in spite of a strong sense of guilt, and about which he had never been able to speak before to anyone. He was opposed as a suitor by the parents of the girl with whom he was in love, because of racial differences and because of his poor financial prospects, and since this problem had come up, his symptoms and his nervousness had become worse, and their exacerbations had finally brought him to the hospital.

After he had revealed his situation and after his physical examination had shown nothing but a spastic colon, the nature of his emotional disturbances was reviewed with the patient and their relation to his symptoms were explained. In a week he reported that he was in a much better frame of mind, that his diarrhoea had been reduced to two movements a day, and he also said that he then understood things that had puzzled him for a long time, feeling at length that he was on the road to recovery. This progress continued, although his love affair went badly and gave him serious disturbances, but about seven months later he wrote: "I have been getting along very well since I saw you and I now feel like a different person. The several talks which I had with you did me a world of good, and in the vernacular of the street, I have become more 'hard-boiled' and I don't let anything worry me any more. I am planning to get married by next spring".

This is a different story from that told by the nervous, anxious, disturbed young man who appeared in the clinic suffering from chronic diarrhoea, with insecurity, frustrations, a disturbed love affair and a sense of guilt because of eroticism. Three interviews, only one of which was lengthy, were required to set this patient on the road to health and greater happiness.

Case 23. A man of sixty-eight had been retired on a small pension by a large utility company ten years before because of poor health. He feared he had cancer at this time, but had soon been convinced after examinations at the Johns Hopkins Hospital that his health was not seriously impaired. He had, however, had a difficult time supporting himself and his wife, and they worried a great deal over their insecurity. About five months before coming to the hospital he de-

veloped some rectal pains and an embarrassing odor of rectal origin, which was subjective and not noticed by others, and which interfered with his efforts to make a living. About a month later, he heard of a book called "Hints on Intestinal Complaints and Troubles", which he obtained at a public library. After reading it, he was convinced he had colitis, and had from then on taken two enemas a day, often devoting an hour to each operation.

The patient responded well to explanations of his illness, and was reassured by his negative examinations. He was no longer annoyed by the idea of a rectal odor, stopped taking enemas, and five months later, he reported that he was entirely well, had had no return of symptoms and had taken an enema not oftener than once a month. There had been no improvement in his financial status.

Case 24. A forty-six year old industrial worker had a fear of gastric cancer, implanted upon long-existing digestive symptoms culminating in a duodenal ulcer. He came to the hospital to get an unprejudiced diagnosis, and he therefore gave a fictitious history, evading his past hospital experiences and the story of his brother's death from cancer. During the interview he suddenly changed his attitude, said that he had deceived the doctors in the clinic, and gave as accurate an account of his illness as he could.

His symptoms started when fighting at the front in the World War, as a protracted diarrhoea which he attributed to faulty diet. He denied excessive anxiety at that time. His digestive symptoms had been present for about twelve years when his brother died in 1930, which was a source of anxiety to him. Soon thereafter he had a gastric hemorrhage and entered a hospital of the Veterans' Bureau, where a diagnosis of duodenal ulcer was made. He was allowed a pension of forty dollars a month on discharge, but continued to have symptoms, the most striking of which was complete loss of hunger sensation, even if he went thirty-six hours without food. This lack of hunger had been present for ten or eleven years, but in spite of it the patient was well-nourished, appeared quite robust, and had been able to carry on as an industrial worker. His brother's death was constantly on his mind, and it was the gradually increasing fear of cancer that had brought him to the hospital.

The patient was much relieved to learn that his examination failed to reveal any evidence of cancer, and he was glad of an opportunity to discuss his situation. He had grown up on a farm in Virginia where he sometimes visited his family, and felt better there than elsewhere. He said he would move there with his family and could take part in the farm activities. His state of mind seemed much improved when last seen, but he could not be followed, as a home visit revealed that he had gone South without leaving his address.

Case 25. A highly trained, thirty-seven year old, unmarried musician, had gone from a small town to a large city conservatory to study music, and had had digestive symptoms at times while there. He had returned to teach music privately in a small city, where there were meagre cultural opportunities, and

where he was dissatisfied and disappointed. His digestive symptoms had been constant for three years since the Sunday his mother, who had been keeping house for him, was killed by an automobile on her way home from church, while he was on his way to meet her. He complained of gastric pains, fatigue and a loss of interest in his teaching, as he was discouraged and felt competent in his work for only about one hour a day. He expressed a fear that cancer might be his trouble. Reassured on this point and given an explanation of the cause of his illness, he was apparently convinced and grateful. Six months later, he wrote that he was distinctly better, and on some days felt entirely well, but that he had a sore spot on his tongue which gave him concern. On this account he wanted to pay a visit to the cancer clinic some time in the near future. Otherwise, he was going on well with his teaching, playing a church organ, and on the whole, was rather contented, if not perfectly happy.

Case 26. A married man of thirty-seven had developed digestive symptoms when he was promoted from locomotive fireman to a job as railroad detective, a position involving an irregular life filled with emotional strain, and requiring clerical duties that were difficult for him. He had a strong feeling of insecurity and expressed concern as to the support of his wife and children in event of his death. He had been given several diagnoses by doctors he had consulted, and when he came to the hospital, had the thought of cancer constantly on his mind. He also feared insanity. A change of job to that of a welder in a steel plant after a full discussion of his illness and its causes, brought about a complete recovery. Six months after his last visit to the hospital, when seen at home, he said that his entire outlook on life was changed, and that he thought his visits to the hospital had saved his life.

Case 27. A young married Italian woman had consulted her family physician because of digestive symptoms and had been told that she had a gastric ulcer. Her doctor evidently recognized the need of reassuring the patient, as he told her that it was not serious and would respond readily to diet. The effect of his reassurance was destroyed, however, by some of her friends who convinced her that a gastric ulcer was incurable. Her symptoms were not relieved by diet, and she came to the hospital complaining of epigastric pain. No evidence of ulcer was found, and she could be given reassurance on a sounder basis than before. Her symptoms soon disappeared, as was reported when a home visit was made a month or so later.

Case 28. A forty-five year old widow, employed as a housekeeper, suffered from chronic constipation. She feared she might have a rectal stricture requiring operation. Her examination revealed a spastic colon, which was apparently related to her emotional reaction caused by the insecurity of her only son, and also by some of the requirements of her work. She was relieved when the nature of her complaints was explained, and she seemed to have achieved an altered

point of view regarding her situation. This patient was not followed long enough to judge the ultimate results.

Two patients in this group were successful, well-trained industrial workers who were disturbed by the loss of the jobs they had filled for a number of years.

Case 29. One was a forty-nine year old steel worker who had, during the course of thirty years, worked up to a highly skilled, well-paid position. He was devoted to his work; and his mill, for which he had an enthusiasm bordering on affection, had shut down some months ago, and he had been transferred to a warehouse job. He said he had developed a sense of failure, which had affected his physical well-being, and although he complained of pain and discomfort in his stomach, he came to the hospital because he wanted to have a physical check-up. His digestive symptoms had apparently set up a vicious circle, as they caused him to worry, which made his symptoms worse. It was evident that an explanation of his symptoms and reassurance regarding his physical condition were sufficient to break the vicious circle, as he reported about ten weeks later that he could find nothing to complain of regarding his health.

Case 30. The other man, who was fifty-seven years old, had been a mechanic for years in a railroad repair shop and had been furloughed six months previously. He had had a burning pain in his epigastrium for some years, and his digestive symptoms had been fairly constant for some months before he stopped work, but as nothing abnormal was found in his digestive tract, his symptoms seemed largely psychogenic, although his blood-pressure was elevated. He was worried about his heart, asked many questions about his health, and had an exaggerated idea regarding the value of drugs. However, with encouragement and explanations his digestive symptoms disappeared almost immediately. It was evident that his anxiety disappeared with a better understanding of his physical condition, for which he was especially grateful. A sense of insecurity, both before and after his retirement, seemed to be the chief source of worry which had resulted in a typical hypochondriacal reaction in a man who seemed superficially well-integrated and without abnormal personality traits.

The three patients with hypochondriacal reactions who did not respond favorably to treatment are the following cases.

Case 31. A young married man of twenty-six, who had had frequent attacks of abdominal pain and discomfort for eighteen months, accompanied by moderate loss of weight and strength, had recently felt depressed. Except for a rapid pulse and an elevated sedimentation rate, his physical examinations were negative.

The patient was a neatly dressed, quiet speaking, rather attractive young man, who seemed to be without anxiety or emotional strain. He told of a dis-

turbed childhood, caused by an antagonism toward his hard-drinking step-father whom his mother had married after his father had been killed in a railroad accident when the patient was six years old. He said he was much attached to his mother and would stick by her "through thick and thin". He had worked for several years on a railroad maintenance gang, living on work trains, but had returned to his mother for care when his symptoms had begun. About six months later he married a girl one year his senior, who was employed as a shoe worker, and since their marriage, which he said was very happy, they had lived in a boarding-house, supported by his wife.

It was difficult to give this patient insight into his illness, except to tell him that no organic disease was discoverable to account for his symptoms. When visited six weeks later, he had just returned from playing in a ball-game, and looked very well. He said he felt well except for pain in his lower abdomen from time to time, and he did not think he could go back to work. He showed no interest in receiving further treatment.

The childhood experiences of this patient gave ample evidence of maladjustment and dissatisfaction, and his present situation strongly suggested that his wife had become a mother-substitute to him. His abdominal symptoms were necessary for the maintenance of this relationship and he seemed to accept them with complacency. It was evident that successful treatment could not be carried out without a more penetrating form of psychotherapy, which he did not desire to receive. He was comfortable with his symptoms, and at least subconsciously, did not want them disturbed. He had apparently a mild character neurosis.

Case 32. Another patient in this group was a young man of twenty-three years who lived in a small town where he could find no work. He was a "neurotic' type, and had become much engrossed in his health from reading so-called health magazines, which had led him to dietary restrictions, dumb-bell exercises and to the use of enemas. He complained of attacks of right-sided lumbar pain, which his family physician could not explain, and for which no cause could be found by gastro-enterologist, surgeon or urologist. This boy was distinctly introspective and "inadequate". He would not seek employment in the largest industry in his town, a fire-works factory, as he said it was too dangerous. Although he said he was better when seen a year later, his improvement was not marked, and he gave the impression that he would develop into a chronic semi-invalid, as he appeared fearful and emotionally unstable. He seemed to lack ability to gain a satisfying state of integration, but a superficial study of his situation failed to reveal concrete problems that could have a causal relation to his complaints and which would serve as a basis for discussion. The patient lived at a distance from Baltimore and was able to make only infrequent visits, so that psychiatric treatment was not practicable.

Case 33. The third patient in this group complained of persistent abdominal pain for which no physical cause could be found. She was a rather simple type of

country girl of twenty years who had had a disturbed and difficult childhood following the death of her mother when eight years old. At the time of admission to the hospital, she was living far from home doing housework for a boarding-house keeper, who had recently become ill with heart disease. The patient showed little or no evidence of anxiety or emotional instability and her pain persisted after she stopped work. After reviewing her physical and social status, it was decided that her symptoms were probably caused by her lack of social outlets and family group relationships. Her lower abdominal pain and soreness were present after weeks of careful study in the clinic, and interviews never revealed any social or sexual problems which the patient would admit as a cause of tension, although she did have unusually heavy work for a girl of her age.

She remains the most obscure diagnostic problem in the series, and is placed in the group of hypochondriacal cases because of the persistence of her complaints and the unsuccessful efforts to find a physical cause for them. She did have one element in her situation that was almost constantly present in relation to hypochondriacal reactions in our patients, a state of insecurity.

The success of treatment in the patients with hypochondriacal reactions seemed to depend upon whether or not a relationship between an emotional disturbance as a cause and digestive symptoms as an effect could be established in the mind of the patients as to the nature of their illness. In nine successful cases this could be done, while in three unsuccessful cases it was not accomplished.

5. Patients with Hysterical Reactions

Three patients who complained primarily of their digestive symptoms gave evidence in their histories of attacks which are considered to be hysterical reactions. All of them had had severe and prolonged emotional strain and in each case periods of apparent unconsciousness were described. They were relatively calm and complacent in spite of the unusually difficult social situations in their lives.

Case 34. A sixty-two year old married woman was brought by her daughter because of spells of persistent nausea, vomiting, and headaches lasting for several weeks at a time, which she had had during the past six years. On several occasions these attacks had brought her to an extreme state of illness, when she had been "given up" by her doctors, as confirmed by one of them by letter. The patient was said to have gone for days without food and to have lain for weeks in a semi-stuporous state. On one occasion all funeral arrangements except a death notice in the newspaper had been made. From these attacks the patient re-

covered suddenly and so rapidly that it seemed miraculous. The patient was cheerful, rather lively and well-nourished, but said that many different foods upset her, and her selection of food was bizarre. Examinations revealed no physical cause for her symptoms. The story of her past and present situation revealed an adequate setting for hysteria, a diagnosis later confirmed by a psychiatric consultation. The patient had had a difficult childhood, as the oldest surviving child of fourteen, and said that she was a nervous, delicate child, much disturbed by frightening dreams which had continued throughout her life. At the age of thirteen she contracted diphtheria, at a time when there were eight children in the family, all of whom except a baby contracted the disease from her, and all died within ten days.

The patient lived in a neighboring state in a small house in the country, where her life was difficult and restricted, especially in the winter time, when she and her husband were more or less cut off from neighbors. Her only child was her daughter living in Baltimore, who had a grown daughter. When the account given by the patient's daughter was put together with her own statements, it was found that the patient developed her severe and dangerous symptoms only when separated from her daughter, and that her miraculous recoveries had taken place when her daughter or granddaughter appeared on the scene. The daughter related how she had been summoned to the death-bed of her mother several times, to find her in extremis, and how on the last occasion, her mother was well enough in ten days to return with her to Baltimore.

The nature of her mother's illness was explained to the daughter, who said that it had been a great puzzle to several doctors who had seen her mother. She was informed regarding her relation to her mother's illness with the hope that she might arrange her life so that the attacks could be avoided, and she was told that hysteria with digestive disturbances is difficult to alleviate, especially when so thoroughly established and when institutional care is not practicable.

Case 35. A forty-nine year old married woman complained of flatulence, loss of appetite and back pains of nine months duration. She also had what she called "epileptic spells" whenever she became unusually nervous. Her physical findings were essentially negative.

At the beginning of the first interview this patient remarked quite cheerfully that she wished she were a writer, as the story of her life would make a "good" novel.

The patient was born in the Middle West of Polish parents and was one of twenty-two children, many of whom had died at an early age. She described her father as a gambling, drunken horse-trader, who beat his children, and when the patient was seven years old her father's house burned down, the patient being badly burned and scarred. She did not go to school, but at the age of twelve ran away to marry a boy of twenty, to escape her father's maltreatment. At seventeen her son was born and four years later her husband was killed. She

was obliged to return to her father with her child, but in two years she was turned out of doors with her son of six years, her fate being similar to that of all her surviving brothers and sisters. After making her way to Baltimore with a brother, and supporting herself for six years, she married a man who lived on an island in the Chesapeake Bay, where he worked as a fisherman. Seven years ago her husband began to lose his vision, and two years later, when he had become almost blind, their house had been washed away by a storm, all their possessions having been lost. Several years ago, the patient lost track of her son, and this situation seemed to have disturbed her as much as her husband's total blindness. She and her husband were living on a blindness pension of thirty dollars a month, in the poorest part of Baltimore, where they were visited.

Her digestive symptoms were complicated by attacks of unconsciousness which were apparently hysterical in nature. It seemed impossible to alleviate this patient's situation, especially as she was resistant to suggestions and not co-operative, although she did seem to gain considerable satisfaction in revealing the story of her tumultuous life. It was not surprising that she should have developed digestive symptoms, which were no doubt brought on in part by the unhygienic conditions under which she lived, and by inadequate diet.

The diagnosis of hysterical reaction was based upon descriptions of her attacks of apparent unconsciousness given by the patient and by one of her neighbors, and also upon the attitude of the patient, her complacency and her relative detachment from her problems, as shown by her remark about writing a novel and her evident lack of desire to be helped.

Case 36. The last case in this group was a sixty-three year old spinster, with abdominal pain, who said that she had transient attacks of unconsciousness which had the characteristics of hysterical reactions, rather than epilepsy. Her physical examination revealed only an absence of her pelvic organs which had been removed at the age of twenty-one by a surgeon in South America. She had had a greatly disturbed life and had broken away from her family twenty-four years ago, when her father remarried soon after her mother's death. She had supported herself by doing domestic work, and at the time of her admission to the hospital she felt insecure, lonely and unhappy, although she appeared to have a naturally buoyant spirit. Her history suggested that she had had a mild hysteria for about ten years, and her symptoms were aggravated by loneliness at the time of admission, because the woman with whom she lived was undergoing hospital treatment. She was economically insecure, lacking in family group and social outlets, and felt a sense of friction and resentment toward her family, as well as much self-pity, which seemed well-grounded. She had moved to another city when an attempt was made to follow up her case by a home visit.

None of these patients was directly benefited by psychotherapy, although in the first case the family situation was adjusted in a way

that might prevent future attacks. All of these patients were in very disturbing situations which could not be radically altered, and their problems lay deeper than at levels to which the psychotherapy went. The detection of hysterical reactions is to be taken as a sign that extensive treatment by a psychiatrist is indicated.

6. Patients with Depression

The two remaining patients were in a state of depression, being discouraged, anxious and with a feeling of incompetence. Both responded well to treatment for a time and then relapsed. It is not a simple matter to decide to what extent depressed patients are benefited directly by any form of therapy, because the variations or swings of mood that take place naturally, may be the true cause of improvement, and may be coincidental with therapeutic efforts, especially if these efforts are maintained long enough. Not too much credit can therefore be taken for the temporary benefits that occurred in these patients.

Case 37. A fifty-two year old West Virginia farmer had developed increasing abdominal pain for a period of two or more years, after having had "indigestion" off and on for about eight years. He had been planning to come to the hospital for about a year, as he was disturbed by the thought that his illness might incapacitate him for farm work, and as his worry had been augmented by a disagreement between the doctors he had consulted. One of them had treated him for a gastric ulcer, no evidence of which could be found at the hospital.

The patient was a quiet, short, thick-set, slow-speaking man, who looked considerably older than his age. He was emotionally unstable and several times during the interview his eyes filled with tears, his face flushed and his voice failed. As a young man he had been a school-teacher for seven years, but had given this up because it was "so hard on his nerves". He gave the impression of having had a hard and rather unsuccessful life. His four children had married and left home, but he was supporting his wife's parents. He said his chief worry began about two years ago, when his digestive symptoms had become worse, because his wife had joined the "Holy Rollers". He was a religious man, a steward of his church and a Sunday-school teacher. He was now disturbed by the fact that when he and his wife drove to town each Sunday, she was no longer by his side in church, but was attending a church of a sect of which he disapproved.

This patient was evidently depressed and felt insecure. He gave the impression that his mental status had been affected by cerebral vascular changes. He spoke of his wife's religious behavior as though his feelings were hurt thereby. He was relieved by a discussion of his negative physical findings and by an effort

to encourage him and to offset his sense of insecurity. He seemed to profit by a discussion of the relation of his complaints to his emotional state, as he reported by letter ten months later that he had felt much better for several months after returning home, but had recently had digestive complaints and was again hardly able to work.

Case 38. The last patient has been followed for over two years and studied recently in collaboration with a psychiatrist, Dr. Leslie B. Hohman. The patient was a thirty-eight year old street-car operator, and when first seen in October 1938, he complained of having had epigastric pain for ten years. He said he worried about everything, but recently especially about having gall-bladder disease. During the past two years he had been having sharp attacks of abdominal pain of short duration, followed by sweating, weakness, nervousness and anxiety. His appendix had been removed six years previously in what he said was an acute attack, during which he was obliged to drive an automobile for several hours in order to reach a hospital. The patient was a rather excitable, somewhat restless man, who talked intelligently and freely, and was anxious to discuss his symptoms. He said he had always been nervous like his father. He had been employed by the street railway company for eighteen years, and his digestive symptoms had begun when his work had been changed from that of conductor to that of motorman. He was operating a "one-man" street car over a route through crowded, busy streets. His fear of gall-bladder disease had been present ever since his superintendent, who had "treated him as a father", had had a gall-stone attack two years ago, and had died following an operation. He had not been able to get this episode off his mind, as the superintendent had always given him much moral support, and the thought of his friend's death had made his symptoms worse.

The more acute attacks of pain which made it difficult for this man to continue with his work, came on most frequently while operating his car, but never forced him to retire immediately. They were more severe and more frequent when the track was slippery or when autumn leaves were on the rails, making the control of his car difficult. His worst recent attack had occurred soon after his car had nearly hit an old woman, an incident, which, he said had given him his "greatest scare in six months". Further experiences were related, all of which indicated that this patient had "lost his nerve" in operating his car, and had developed typical anxiety attacks, although he had made the unusual record of going an entire year without an accident. His symptoms were evidently precipitated by the strain of his daily work, and he had also developed anxiety regarding his diet and the sort of place in which he ate.

His situation was analysed with him at the end of the second interview, when he could be assured that he had no organic disease, but that his symptoms could be definitely accounted for by his attitude regarding his work. He was told that he needed to change his attitude for the sake of his health. This he succeeded

in doing by following instructions and in a month he reported enthusiastically that he was no longer worrying, had a much calmer attitude, was eating without restrictions and had gained eight pounds in weight. He was so gratified by his improvement, that he was warned to expect digestive symptoms or anxiety attacks in the future, but that he should not be unduly concerned about them. Reassurance was augmented by a visit to his home, and by a talk with his sensible and congenial wife. They had no children, although married about fourteen years, and had taken no contraceptive precautions.

Eight months later the patient said that after a summer in the country he had remained perfectly well except for indigestion on some days after insufficient sleep because of late night runs on his street car, and he seemed elated by the marked change in his health. About four months later, however, he reported that he was again feeling the strain of his work, and with the cooperation of the company doctor, his work was changed to that of conductor on a relatively quiet suburban run. After a few weeks of this work, he complained of being bored and depressed by the relative inactivity of his work and asked to be put back on his old run, which he said was an "enticing job".

His life in his old job went well for a time, but he began to feel depressed again and after he had been at it for three or four months, his wife appeared in the clinic to ask for advice, as he had been much disturbed for three weeks. He was very restless, excitable and had turned on his wife with accusations of infidelity and seemed to have lost control of himself at home. She related that this striking exacerbation of symptoms had followed a shocking episode. One of his fellow employees, an intimate friend, had boarded his car to ride from the car-barn to the office to turn in his receipts for the day. When the car was stopped at the usual place, the friend did not get off, and when the patient went back to him, he found that he was dead.

The wife brought the patient to the hospital within the next few days, and he recounted the episode, telling how he had to carry out various procedures while the car-line was tied up, and how he finally carried the corpse to an ambulance unassisted, feeling that it was as "light as a feather". He then felt exhausted and unstrung, and had felt under tension, restless and irritable ever since.

The patient was seen subsequently with Dr. Hohman, and an effort was made to obtain an account of the various mood swings the patient had experienced. This was not very successful, as he could not think about himself or express himself in terms of moods.

It was interesting to discover at this time that a brother of the patient was under treatment in the psychiatric dispensary for a depression, and gave a history that paralleled that of the patient closely. The brother was about eighteen months younger than the patient, and like him, had come to Baltimore from a farm in Virginia and had worked for eight years as a street-car operator, but had given up the work as being too hard on his nerves.

The patient proposed that he return with his wife to the family farm in Vir-

ginia where he had always felt very well, and where he had previously taken prolonged beneficial vacations. He denied convincingly any thought of suicide and the plan was approved.

This case was at first thought to be especially favorable for treatment, as the patient responded so rapidly and enthusiastically to the first interviews. In the light of subsequent events, however, it became clear that the patient had a true depression complicated by anxiety attacks, suggestive of a manic-depressive psychosis, with a poor prognosis for more than temporary recovery. The patient was unable to stand up to the daily emotional strain of his work without excessive reactions, and succumbed more or less completely to the shock of particularly disturbing episodes.

DISCUSSION

The frequency and character of the personality disorders occurring in patients with gastro-intestinal complaints are indicated by the thirty-eight cases that are reported. These patients have been treated by a simple form of psychotherapy by an internist without any special training in psychiatry, and an effort has been made to determine which patients responded favorably to this form of treatment and which did not. Twenty-three of the patients are considered to belong in the favorable group. These patients were in general terms conscious of their problems, able to relate them to their digestive complaints and without much disturbance or distortion of personality. They were patients with "situational neuroses", who could be given sufficient insight, guidance and encouragement in a few interviews to enable them to solve their problems or adjust themselves to their problems to an extent sufficient to relieve their digestive complaints. This relief of digestive symptoms, when such relief seemed to be permanent, was taken as the criterion of a favorable result.

The patients in whom these results were obtained were those having excessive emotional reactions, anxiety attacks or hypochondriacal reactions. Of the twenty-nine patients in these groups, all but six responded favorably to treatment. Of these six, two with excessive emotional reactions were facing difficult social situations which could not be relieved. Another patient primarily disturbed by a situation causing constant frustration, was mentally retarded and was unable to gain an understanding of his problems. There were also three patients with hypochondriacal reactions who were not satisfactorily relieved. One of them had persistent abdominal pain which served

to maintain him in a social situation that was satisfactory to him, and he did not seem interested in being relieved. The other two apparently had personality disturbances or "character neurosis" that could not be satisfactorily revealed or treated.

There were seven patients grouped as having general nervousness, hysterical reactions or depressions who showed no lasting improvement of their digestive complaints. The four with general nervousness had life-long histories of emotional instability and seemed to be "unmodifiable material", their digestive symptoms being one of the signs of their inability to face the normal situations of life. The three patients with hysterical reactions did not receive permanent benefit. One of them had had rather severe hysterical symptoms over a period of years, a diagnosis confirmed in the psychiatric clinic, while the other two had been facing for years extremely severe social adversity with much emotional strain. One of these patients was uncooperative, partly because of the difficulty of coming for treatment, while the other patient moved away from Baltimore before treatment could be given a fair trial.

Of the two patients with depression, one returned after a short stay in Baltimore to his home in West Virginia, while the other has gone through a fairly typical course of a manic-depressive psychosis, after recovering rapidly from his digestive symptoms when first seen, but with later recurrence.

A question frequently raised by patients with personality disorders, especially in hospital practice, is whether or not they should be referred to a psychiatrist. It is often not a simple question to answer. Psychiatrists say that many patients with simple depressions, anxiety or hypochondriacal reactions should be successfully treated by the internist or by the family physician, and they urge that intelligent efforts should be made to do so. The study of our patients strengthens the conviction that in an out-patient department, patients with minor personality disorders should be considered the responsibility of the doctor to whom they are initially referred, and that he should retain this responsibility until he is convinced by a serious trial that he cannot treat their personality disorders successfully. This question has been recently discussed from the psychiatrists' point of view by McGraw (8), who emphasizes the importance of an intimate

individual doctor-patient relationship as necessary for gaining an understanding of the personality disorders of patients. It is his opinion that a reason for referring a patient to a psychiatrist, when personality factors are considered, "should be based on an honest recognition of a failure to be at ease in the presence of the problem". The important point is that the personality disorders should be treated seriously and not lightly put aside, especially in a gastro-intestinal clinic.

The study and the treatment of personality disorders of patients with digestive complaints should be considered as preventive medicine. Many patients have digestive symptoms as a manifestation of a personality disorder before they develop organic lesions of the digestive tract, which might be prevented if their personality disorders were successfully treated. This point is brought out by a study by Brown and Dolkart (9) who reviewed 1500 cases of recurrent peptic ulcer. After an effort to evaluate honestly the causative factors of the disease, they conclude that "functional nervousness including fatigue and anxiety, was by far the greatest detectable cause of recurrence", and that in many instances it seems quite plausible that the same etiological factors were also responsible for the original ulcer. It is of interest to ask the question as to how many of these patients might have escaped peptic ulcers if their "functional nervousness" had been successfully treated in the first place.

From the point of view of mental hygiene, the value of the study of the patient as a person is well illustrated by this series of cases. Personality disorders were discovered because the patients sought relief for their digestive complaints, and it was these disorders, rather than diseases of the digestive tract, that were of primary importance both from the diagnostic and from the therapeutic viewpoint in a large majority of the cases.

SUMMARY

Fifty patients admitted consecutively to the Gastro-intestinal Clinic of the Johns Hopkins Hospital Dispensary were studied with the object of determining the significance of social problems and emotional disturbances as a cause of digestive complaints. Thirty-eight patients in the series were found to have personality disorders

of which their digestive complaints were an outstanding symptom. In most cases these patients had no demonstrable organic lesions to account for their digestive complaints.

The personality disorders of these patients have been studied and grouped according to their characteristic features, and have been treated by a simple form of psychotherapy which is described. Twenty-three patients responded favorably to this form of therapy and fifteen did not. These cases raise the question as to what types of personality disorders should be treated by the gastro-enterologist or internist, and what types should have psychiatric treatment. This question is discussed.

The records of these patients are reported in order to indicate the characteristics of the personality disorder and the results of treatment in each case.

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INFLUENCE OF ESTRIN ON CALLOUS FORMATION

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In June, 1939, Doctor Fuller Albright, of Boston, talked to the Johns Hopkins Medical Society about bone physiology. On that occasion, he discussed the work of Gardner and Pfeiffer (1) on pigeons. These workers found that during ovulation the long bones ordinarily become somewhat decalcified and consequently more permeable to x-rays. The calcium is presumably taken from the bones for the formation of the egg shell. Administration of estrogenic substances to pigeons during ovulation will produce an increased density of bone. Even in male pigeons, the density of the bones can be increased by the administration of estrogenic substance. These authors also reported that the level of the blood calcium was raised by the injection of estrin. Geschickter (2), and Levin and Smith (3) have shown that in mammals the blood calcium level cannot be elevated by the injection of estrogenic substances.

Stimulated by Doctor Albright's exposition, we decided to test the effect of estrin upon the healing of fractures. Our results are shown in the following three case reports, and in experimental studies of animals having artificial fractures.

CASE REPORTS

Case 1. B. B.: A white female, aged 70, whose past history is unimportant, fell on May 6, 1939 injuring her right forearm. X-ray showed a fracture of both the radius and ulna at the juncture of the middle and upper thirds, with lateral displacement. The fractures were reduced by Doctor Douglas Stone, at the Union Memorial Hospital and the arm was put in a cast. Repeated x-rays up to July 3, 8 weeks after fracture, showed no callous formation and there was no clinical evidence of union. Beginning July 17, *Theelin* (2,000 units hypodermically) was administered three times a week. On July 31, 2 weeks later, x-ray showed beginning callous formation. *Theelin* was continued and on August 18, x-ray showed marked increased callous formation. The patient went on to a complete and uneventful recovery.

Case 2. M. H.: A 30 year old married white woman, whose past history is non-contributory, fell down stairs on July 9, 1939 and fractured her right humerus in the middle third. The fracture was reduced by manipulation and the arm was

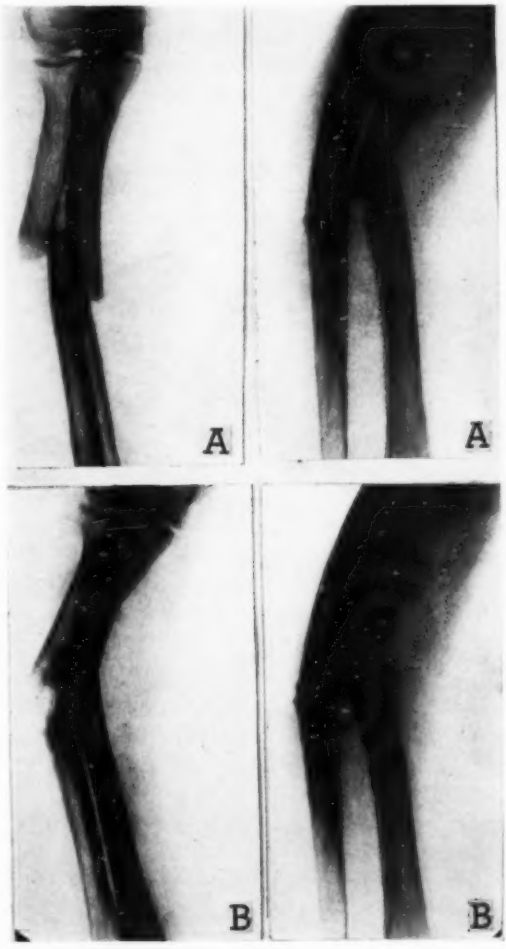

FIG. 1. Case 1. A. X-ray pictures taken July 3, 1939, 8 weeks after fracture. No callous formation. B. X-ray pictures taken August 18, 1939, after 4 weeks of estrin therapy. Note callous formation.

put up in a plaster cast. Within a few days the patient developed a radial nerve palsy and on July 12, an open reduction was done by Doctor Douglas Stone at the Union Memorial Hospital; the fracture was reduced and held in place with a Lane plate. She was discharged on July 21, in good condition. Repeated x-rays up to December, 1939, 6 months later, revealed no evidence of callous formation. Several doses of *Theelin* were given in December, but it was not given regularly until December 31, when 10,000 units were administered 3 times a week up to January 31, 1940, a total of 130,000 international units. X-rays taken at that time showed evidence of beginning callous formation. *Theelin* was continued at the rate of 30,000 units per week. By March, there was considerably more callous formation and evidence of clinical union. Healing continued in this case slowly but definitely and she left the city in May. At that time a cast was no longer necessary, though the arm was supported in a sling.

Case 3. M. H.: A white female, aged 19, fell from a horse in October, 1937, fracturing her left tibia and fibula. Gas gangrene developed and amputation was considered. This was not necessary and recovery took place, though the fracture did not unite.

The only significant point in the past history is that the patient, a large girl 69 inches tall, weighing about 170 pounds, had always menstruated irregularly. She usually had no more than eight periods a year. The last menstrual period before the operation in May, 1940, was March 5, 1940.

In January, 1938, a sliding graft was done by Doctor Robert Johnson which failed to produce union. From January to May, 1940, *Theelin*, 2,000 international units (0.2 mgm.) was administered once a week without any visible results.

On May 24, 1940, Doctor Johnson removed a graft from the right tibia and placed it in the left tibia at the site of the fracture. *Theelin*, 10,000 units (1 mgm.) per dose, was started one week after operation, and was given 3 times a week. This program was continued during June and July. Beginning in August, *Antuitrin-S* was substituted for *Theelin* the first two weeks after each period. During this time the periods occurred regularly around the first of each month. Five weeks after operation x-ray showed absorption of the bone graft. Nine weeks after operation the first visible callous appeared in the x-ray. Callous increased and clinically the bone became solid. About 4½ months after operation healing had progressed still further and is apparently continuing.

EXPERIMENTAL

An experiment was started in the Surgical Hunterian Laboratory of the Johns Hopkins Medical School on October 20, 1939 to determine the effect of estrin on fracture repair. Thirty-one cats were operated upon and 13 were carried to completion, the other 18 dying of distemper, infection and unexplained causes. The completed

series consisted of three spayed females, one castrated male, one normal male and eight normal females (see protocols).

The cats were anaesthetized with nembutal and ether. The right foreleg was shaved, and cleaned several times with alcohol. The middle third of the radius was exposed without cutting any muscle fibers and the bone was divided in the central portion with the bone cutter. The muscles were then approximated. The skin was closed with subcuticular sutures of fine silk and liquid adhesive was applied to the wound. We relied upon the ulna for splinting purposes and applied no casts or external splints of any kind. X-rays of the right leg were then taken from the second to the sixth week postoperatively.

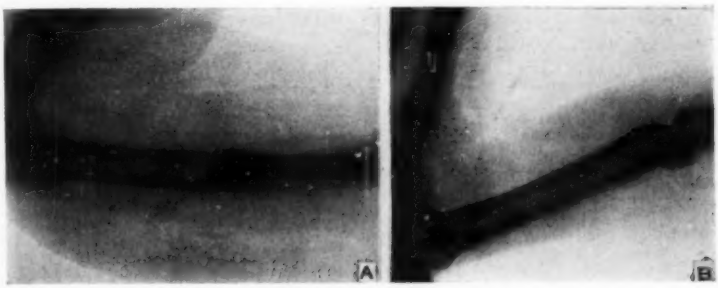

FIG. 2. Case 2. A. X-ray picture taken December 31, 1939, 5½ months after fracture. No callous formation. B. X-ray picture taken March 27, 1940, after 3 months of estrin therapy. Note callous formation.

After an appropriate interval, usually six weeks, the left radius was divided in a similar manner and the cat was given (usually biweekly) intramuscular injections of *Theelin*.[1] X-rays of the left leg were then taken from the second to the sixth week, inclusive. We were then able to compare callous formation at corresponding intervals in similar bones of the same animal with and without estrin therapy.

After completion of the experiment, the x-ray plates were shown to Doctor George Bennett. He was asked to compare the corresponding legs without previous knowledge as to which was the treated side. In each of the first nine animals, he picked the treated side as showing

[1] *Theelin* was supplied by Parke Davis and Company for the animal experiments.

earlier and more extensive callous formation. Of the remaining four, three were considered to show greater callous formation on the untreated side; one showed the same degree of callous formation in the two legs. The last seven cats in the series had received a total average dose of over 20,000 units each, while the first six had received less than 10,000 units each.

Albright's (4) recent experiments on osteoporosis of the spine have shown that it is possible to produce a positive calcium balance with small doses of estrin, but that large doses of estrin may produce a

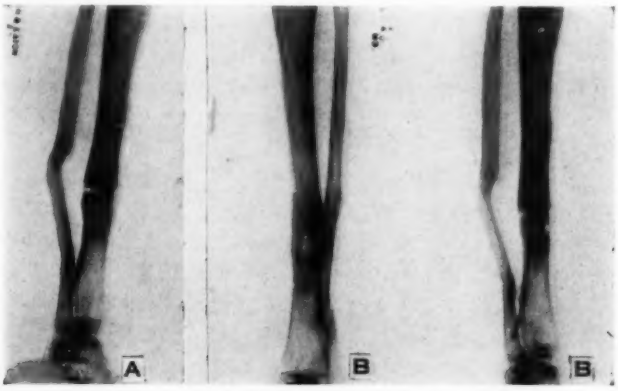

FIG. 3. Case 3. A. X-ray picture taken July 28, 1940, 5 weeks after bone graft, showing absorption of graft. Patient had received some estrin prior to this picture. B. X-ray pictures taken October 5, 1940, after continuous estrin therapy. There was solid union of the fracture at this time.

negative calcium balance. We have discussed dosage with Doctor Albright and find that he gives 10,000 to 30,000 international units per week to the average 150 pound patient. Our dose of 2,000 to 4,000 international units per week to a 3 pound cat would be approximately five to ten times as large.

Because of Albright's (4) findings, we thought that the higher doses of estrin in the later cats might have constituted an over-dosage in some cases. Our most impressive result had been obtained in the normal male cat. This cat was the largest in our series which again might suggest that the amount of estrin given is important. Dosage

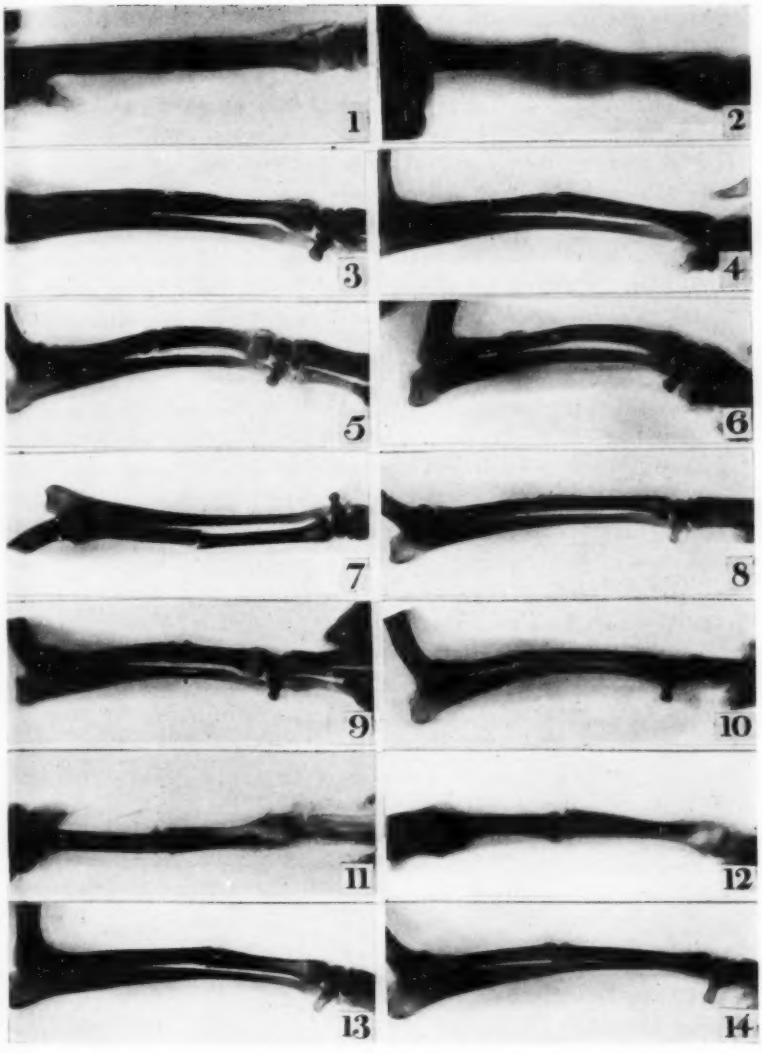

FIG. 4. X-ray pictures of the legs of the 7 dogs treated with estrin. The estrin-treated (left) legs are shown in the right hand column with the corresponding control (right) legs opposite them in the left hand column. The pictures of the estrin-treated legs were taken 28 days after fracture, those of the control legs 29 days after fracture. Although the difference between the two legs cannot always be easily detected in single x-rays, callous formation was considered to be greater in the left leg in all except one animal (pictures 9 and 10).

had not been very accurately controlled in our experiment. Nevertheless, in the series of 13 cats, the results were interpreted as positive in 69 per cent of the animals, irrespective of dosage.

In April, 1940, Pollock (5) published results of his experiments on the effect of *Theelin* on fracture repair. Pollock (5) used spayed rats varying in age from 6 months to $1\frac{1}{2}$ years. He found that spayed rats showed practically no callous formation in 21 days after fracture but 75 per cent of the spayed rats showed callous formation in 21 days if given large doses of *Theelin*. This work was published before our cat experiments had been completed.

Since our experiments on cats and Pollock's experiments on rats had not been uniformly successful, another experiment was started in August, 1940. Seven *dogs* were weighed carefully so that an accurate dose of *Theelin* could be administered. Three normal females and four normal males were used. The experiment (see protocols) was carried out precisely as the cat experiment had been. *Theelin* was given bi-weekly: the first three doses were equivalent to 20,000 international units for a 150 pound adult and the last nine doses were the equivalent of 10,000 units bi-weekly for a 150 pound adult. Six of the seven dogs showed more callous formation on the treated side after 3 to 5 weeks of treatment. The seventh, a female, showed more callous on the control side (see figure 4, pictures 9 and 10). This dog gave birth to two normal puppies several days before the left leg was fractured. The dog was pregnant during the healing of the control side. We shall not attempt to explain the result obtained in this dog, though it is possible, as Doctor John Eager Howard has suggested, that this dog had more estrin in its circulating blood while the control leg was healing, than it had during the subsequent period of *Theelin* injections.

DISCUSSION

It should be noted that in the animal experiments, the effect of estrin upon callous formation was neither as striking nor as uniform as we had anticipated that it might be. The number of animals used in the experiments was not large, and the occurrence of greater callous formation in even a small percentage of the control legs makes one cautious in interpreting the results. The effect of the estrogenic

material upon the three patients cited, appeared to be more striking than the effect upon the animals. The difference may have been due to the fact that in the patients we were attempting to rectify a a definitely abnormal type of bone repair, whereas in the animals we were attempting merely to exaggerate the normal process of healing.

PROTOCOLS

A. Cats

1. Female. Ovaries removed October 20, 1939. Fracture, right leg, November 17, 1939. Fracture, left leg, December 15, 1939. *Theelin* 9,000 units given between December 18, 1939 and January 5, 1940.

2. Male. Previously castrated. Fracture, right leg, November 17, 1939. Fracture, left leg, December 8, 1939. *Theelin* 12,000 units during next three months.

3. Female. Ovaries removed November 10, 1939. Fracture, right leg, December 1, 1939. Fracture, left leg, December 15, 1939. *Theelin* 9,000 units between December 18, 1939 and January 5, 1940.

4. Female. Ovaries removed November 24, 1939. Fracture, right leg, December 6, 1939. Fracture, left leg, December 20, 1939. *Theelin* 2,000 units in single injection January 2, 1940.

5. Female. Normal. Fracture, right leg, January 5, 1940. Fracture, left leg, February 16, 1940. *Theelin* 16,000 units between February 16, 1940 and March 21, 1940.

6. Male. Normal. Fracture, right leg, January 5, 1940. Fracture, left leg, February 16, 1940. *Theelin* 16,000 units between February 16, 1940 and March 21, 1940.

7. Female. Normal. Fracture, right leg, February 2, 1940. Before the time of the second operation the animal developed distemper and was very ill but finally recovered. Fracture, left leg, April 19, 1940. *Theelin* 22,000 units between April 19, 1940 and May 26, 1940.

8. Female. Normal. Fracture, right leg, February 9, 1940. Fracture, left leg, March 15, 1940. *Theelin* 24,000 units between March 15, 1940 and April 26, 1940.

9. Female. Normal. Fracture, right leg, February 23, 1940. Fracture, left leg, March 29, 1940. *Theelin* 20,000 units between March 29, 1940 and May 10, 1940.

10. Female. Normal. Fracture, right leg, March 1, 1940. Fracture, left leg, April 5, 1940. *Theelin* 20,000 units between April 5, 1940 and May 15, 1940.

11. Female. Normal. Fracture, right leg, March 1, 1940. Fracture, left leg, April 5, 1940. *Theelin* 20,000 units between April 5, 1940 and May 15, 1940.

12. Female. Normal. Fracture, right leg, March 8, 1940. Fracture, left leg, April 19, 1940. *Theelin* 22,000 units between April 19, 1940 and May 28, 1940.

13. Female. Normal. Fracture, right leg, March 8, 1940. Fracture, left leg, April 19, 1940. *Theelin* 22,000 units between April 19, 1940 and May 28, 1940.

B. Dogs

1. Female. Normal. (See Figure 4, pictures 1 and 2.) Fracture, right leg, August 6, 1940. Fracture, left leg, September 13, 1940. *Theelin* 16,750 units between September 13, 1940 and October 21, 1940.

2. Male. Normal. (See Figure 4, pictures 3 and 4.) Fracture, right leg, August 6, 1940. Fracture, left leg, September 13, 1940. *Theelin* 16,750 units between September 13, 1940 and October 21, 1940.

3. Male. Normal. (See Figure 4, pictures 5 and 6.) Fracture, right leg, August 6, 1940. Fracture, left leg, September 13, 1940. *Theelin* 15,000 units between September 13, 1940 and October 21, 1940.

4. Male. Normal. (See Figure 4, pictures 7 and 8.) Fracture, right leg, August 6, 1940. Fracture, left leg, September 13, 1940. *Theelin* 15,000 units between September 13, 1940 and October 21, 1940.

5. Female. Pregnant. (See Figure 4, pictures 9 and 10.) Fracture, right leg, August 6, 1940. Fracture, left leg, September 13, 1940. *Theelin* 15,000 units between September 13, 1940 and October 21, 1940.

6. Female. Normal. (See Figure 4, pictures 11 and 12.) Fracture, right leg, August 6, 1940. Fracture, left leg, September 13, 1940. *Theelin* 12,000 units between September 13, 1940 and October 21, 1940.

7. Male. Normal. (See Figure 4, pictures 13 and 14.) Fracture, right leg, August 6, 1940. Fracture, left leg, September 13, 1940. *Theelin* 16,750 units between September 13, 1940 and October 21, 1940.

SUMMARY

1. Three human cases of fracture with delayed union were treated with estrogenic hormone and showed signs of increased callous formation at the site of fracture.

2. Experiments were performed on cats and dogs to determine the effect of estrin on the rate and amount of callous formation following artificial fractures.

3. Although the results in the animals were not uniform, and although the positive results were not always striking, 9 out of 13 cats and 6 out of 7 dogs showed earlier and more abundant callous formation under estrin therapy.

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EXPERIMENTAL STUDIES ON INTRANEURAL SPREAD OF POLIOMYELITIS VIRUS[1]

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The possibility of inducing poliomyelitis experimentally by inoculation of peripheral nerves has been thoroughly established since the pioneer studies of Landsteiner and Levaditi ('09), Flexner and Lewis ('10), and Leiner and von Wiesner ('10). These workers, along with Römer ('13), who first offered evidence showing that the virus spreads preferentially along nerve fiber tracts in the central nervous system, assumed however that the virus utilized lymphatic channels in its spread along these pathways. Since then, the experiments of Hurst ('30), Fairbrother and Hurst ('30), and many others, not only have demonstrated convincingly that the virus of poliomyelitis does spread along nerve fiber pathways throughout the nervous system, but have also suggested that it is the axis-cylinder and not its sheaths or "perineural lymph spaces" which plays the greatest role in this process of dissemination (Hurst, '36, Bodian and Howe, '40b).

Pette ('26) has reported that trauma to a peripheral nerve during intraneural inoculation facilitates "takes" with herpes virus, and the similar finding by Fairbrother and Hurst ('30) for poliomyelitis virus tends to confirm this conclusion. Evidence of a more general nature (Goodpasture and Teague, '23; Goodpasture, '25a and '25b, Pette, '26 and '30, Sabin, '37, and others) further indicates that the mechanism of progression along nerves of neurotropic viruses in general is probably quite similar. Nevertheless, critical evidence that the virus travels within the substance of the axons, rather than along the sheaths of nerve fiber bundles has been conspicuously lacking (O'Leary, et al., '32; Perdrau, '37; and Doerr, '39). That a positive resolution of

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this problem is of the utmost significance in achieving an understanding of the mechanism of growth and spread of "neurotropic" viruses is obvious; up to the present time, however, no attempt has been made to analyse experimentally the separate capabilities of various components of a nerve for the transmission of a neurotropic virus. It is the purpose of this report to describe experiments which have been designed to determine whether or not the virus of poliomyelitis is transmitted within the substance of the axis-cylinder, rather than along any other components of the peripheral nerve or within tissue spaces between the formed structures in the nerve. Some forty adolescent rhesus monkeys were used for the experiments to be described.

METHODS

It is evident that there are two necessary conditions for a critical analysis of this problem, first, a thoroughly reliable method of intraneural inoculation, and second, a method for dissociating experimentally the axis-cylinder from the non-neuronal components of the nerve. The first condition was satisfied by the development of a highly successful method of inoculation which involves no mechanical injection pressure and which places the virus in contact with every fiber at a single level in the nerve (Bodian and Howe, '40a). This is accomplished by sectioning the nerve with sharp scissors and then immersing the central cut end in as little as 0.1 cc. of 20 per cent virus suspension (spinal cord) for 5–10 minutes. Possibly because of the fact that during the first few days after nerve section the nerve cells with axons cut are more susceptible to virus than normal cells (Howe and Bodian, '39), this method, except under certain artificially controlled conditions to be described below, was found to be invariably successful when strains of known potency were used in inoculating large nerves, such as the sciatic, which was the nerve of choice for these experiments. In all subsequent statements in this report the unqualified term "inoculated" implies this method of intraneural inoculation.

It was thought that the second condition, namely separation of the axons from the non-axonal elements in the nerve could be fulfilled by utilization of the phenomenon of Wallerian degeneration, produced by freezing the nerve at a single point with a wedge-shaped piece of carbon-dioxide ice. This method produces complete degeneration of axonal processes and their myelin sheaths peripheral to the point of freeze, without interrupting the physical continuity of the nerve, or seriously affecting its blood supply. Moreover, the connective tissue sheaths and Schwann sheaths of the nerve are not irreparably injured, and are rapidly reconstituted, at the point of freeze, so that continuity of these structures may exist from spinal cord to end-organs at a time when the axons themselves extend only from the spinal cord to the point of freeze. According to the requirements of

individual experiments, time can then be allowed for progressive regeneration of the axis cylinders peripherally from the point of freeze.

Segments of the nerves used in these experiments were taken postmortem for histological study with the gallocyanin method of Einarson ('32), and the silver method of Bodian ('37). Whenever it was necessary to determine the physical status of the nerve at the point of inoculation, for example when regeneration was in progress, the peripheral stump at the point of inoculation was biopsied, fixed in formalin, and stained by the aforementioned methods.

EXPERIMENTS

Series 1. Successful inoculation by immersion of central cut ends of normal nerves, and of nerves with one or two previous peripheral transections

To determine the reliability of the inoculation technique, twelve experiments were performed with the nerve of choice, the sciatic nerve of the rhesus monkey. This nerve was sectioned with sharp scissors near the greater trochanter or at the mid-thigh level, and the central cut end then immersed in as little as 0.1 c.c. of 20 per cent virus suspension for several minutes. In five cases the sciatic nerve had been sectioned peripheral to the point of inoculation two to six weeks previously. In two cases the nerve had been frozen twice, with a two week interval, previous to inoculation above the point frozen. Paralytic poliomyelitis resulted in all cases after an incubation period of 4–6 days. In ten cases the Rockefeller MV strain was used; in one case, the Wfd strain (Trask and Paul, '36); and in one case, inoculation was done with cord suspension of a chimpanzee which became paralysed after inoculation with human stool (Howe and Bodian, '40). Usually the leg on the side of inoculation was completely paralysed on the fifth day. It was also invariably the first member to show poliomyelitic paralysis, followed by the other leg.

These preliminary experiments demonstrated the reliability of the mode of inoculation, and all subsequent experiments were performed with the same potent and homogeneous sample of MV virus which had been kept in sealed ampules at −78°C. It is also clear from these experiments that a previous single transection of the nerve peripheral to the point of inoculation or even two comparable interruptions by freezing, with a two week interval, have no effect on the success of the inoculation, nor do they enhance or decrease suscepti-

bility, in spite of the fact that it has been shown that many of the anterior horn cells are relatively resistant to the virus after intranasal inoculation at a similar period following section of their axons (Howe and Bodian, '39). In view of this fact, it was interesting to note the effect on chromatolytic cells produced by inoculating them directly with the virus by means of the method described. No anterior horn cells are spared when the sciatic nerve is inoculated without previous manipulation. After a single previous cut and inoculation above the cut seventeen days later, the resulting poliomyelitis destroys most of the chromatolysed cells as well as all the unchromatolysed cells, but some chromatolysed cells are spared. These are far less in number than those spared after intracerebral inoculation during the same phase of chromatolysis, so that it appears that the concentration of virus plays a role in determining the degree of sparing of chromatolysed cells (see also Howe and Bodian, '39 and '41). When the sciatic nerve is inoculated above a cut made six weeks previously, the sparing of anterior horn cells is negligible, possibly due in part to the fact that many axons have regenerated to a considerable extent by this time and are less refractory than at an earlier period after nerve section.

Series 2. Failure of inoculation peripheral to point of freeze in sciatic nerve

To test whether or not physical continuity of a nerve, in the absence of normal axons within it, is a sufficient condition for transmission of the virus to the spinal cord, the following experiment was performed: the right sciatic nerve was exposed aseptically near the greater trochanter in two rhesus monkeys. It was then frozen at a single point by pressing a wedge-shaped piece of carbon-dioxide ice against the nerve until its circumference was perceptibly whitened and solidified. This usually involves a segment of nerve about 2–3 mm. in length, and when the ice is removed the nerve resumes its normal appearance and physical consistency at this point.

Following freezing of the sciatic nerve at the greater trochanter level, the nerve was immediately exposed at the midthigh level, sectioned and inoculated in the manner described. In addition to the two animals mentioned, three control animals were inoculated similarly during the next two hours. All five animals were inoculated with

virus-containing material from a single ampule, containing 0.25 c.c. of a 20 per cent cord suspension in distilled water. All three control animals were paralysed on the fifth day after inoculation. The animals with frozen sciatic nerves failed to develop paralysis, fever, or any other outward sign of poliomyelitis. The experiment was subsequently repeated on two additional monkeys with the same result.

This experiment strongly suggests that an intact axis-cylinder is necessary for transmission of the virus along a nerve to the central nervous system. During the first few days after freezing of the nerve, the axis-cylinders and their myelin sheaths undergo degeneration and fragmentation peripheral to the point of freeze, whereas the sheath cells, connective tissue, and vascular structures remain. In the region of freezing many sheath cells appear to recover and survive, but at the margins of the frozen area there is a proliferative reaction of these elements. The nerve central to the frozen portion appears to be morphologically unchanged. It may be argued that although the continuity of the nerve has not been interrupted, and the sheath cells survive the freezing, at least in part, the tissue spaces and vascular and lymphatic channels may have been obliterated in the region frozen, thus preventing passage of the virus by means of these channels across the frozen segment of nerve. The following experiments were then performed in an attempt to overcome this objection, although it seemed likely from the foregoing results that mere physical continuity of, and probably also the existence of tissue spaces in, the various sheaths surrounding the axis-cylinders is not adequate for spread of infectious quantities of virus along the nerve.

Series 3. Failure successfully to inoculate the sciatic nerve below frozen area after regeneration, up to five weeks' duration

It was expected that inoculating the nerve by the transection-immersion method a short distance below the frozen segment, after allowing sufficient time for regeneration of axis-cylinders to the point of inoculation might result in successful infection with poliomyelitis virus. Such was not the case. Inoculation two weeks, five weeks, and six weeks after freezing, at distances of 6, 4, and 2 cm. below the point of freeze failed to produce poliomyelitis. Biopsy and staining

of a segment of the nerve at the region of inoculation in each case revealed that there were abundant regenerating fibers present (compare figs. 1 and 2).

Two possibilities suggest themselves as a result of this experiment. First, if the virus spreads within the axis-cylinders, it must be assumed that the regenerating axon is not as favorable for this spread as are normal axons. This might be due to altered metabolism of the regenerating fiber or to differences in the caliber of the fibers, since all of the regenerating fibers at the time of inoculation were much smaller in diameter than normal axons (see fig. 2). Second, if the virus utilizes non-axonal pathways in the nerve in its spread to the central nervous system, it is conceivable that these pathways have been disturbed by the freezing and the process of degeneration of axons and myelin sheaths, and have not had sufficient time for reconstitution. The fact that inoculation 2 cm. below the region of freezing five weeks after freezing, at a time when reconstitution of the architecture of the nerve in this area is far advanced, fails to produce poliomyelitis suggests of course that it is the axis-cylinders which are refractory, rather than extra-axonal channels. This supposition is verified by the experiments described in *series 5*, below.

Series 4. Results of inoculation of sciatic nerve below frozen area after regeneration of at least ten weeks' duration

When the sciatic nerve is inoculated below the frozen area as late as ten weeks after the time of freezing, new factors appear to determine the result. Of three animals treated in this manner, two succumbed to poliomyelitis after 4 days, while the third failed to show any signs of the disease. A fourth animal inoculated below the frozen area sixteen weeks after freezing also succumbed to poliomyelitis after 5 days. In the latter animal far advanced regeneration of the nerve, along with functional recovery of the limb, had occurred (fig. 3), and it has elsewhere been shown that the anterior horn cells at this time are again susceptible to virus descending through the spinal cord (Howe and Bodian, '41).

At the period of about 10 weeks after freezing, a considerable number of fibers of the sciatic nerve have completed their regeneration, so that it may be presumed that in the two animals who succumbed to

inoculation these regenerated fibers were sufficiently numerous to transmit an infective dose. The failure of the third animal to succumb suggests that the number of fibers capable of transmitting virus at this period is close to the critical number necessary to carry an infective dose.

Series 5. Refractoriness to virus of anatomically intact central stump during regeneration following at least three transections of the nerve

The experiments now to be described were performed in order to determine whether the resistance of the nerve cell to virus can be enhanced by successive freezing or sectioning of the nerve, to a point where inoculation of the nerve central to any point of previous manipulation might be unsuccessful. It is a surprising fact that this result, suggested by the previous experiments, is possible, providing that the nerve is frozen or sectioned at least three times, at about two to three weeks intervals, peripheral to the point of inoculation. Since the nerve is structurally intact central to, and at the point of, inoculation, the only possible interpretation of refractoriness to inoculation is that the axis-cylinders and the cells in which they originate are sufficiently altered by the successive peripheral injuries, so that they become more highly resistant to virus than they are after a single axonal injury (see figs. 4, 5, and 6). It will be recalled (series 1) that after one previous nerve section or two previous nerve freezes the nerve central to the cut or freezes is just as susceptible to virus inoculation as a normal nerve (seven cases). From these facts it follows that the various sheaths in the peripheral nerve play no role, or a negligible one, in the transmission of virus, since in these experiments, although the sheaths and vascular and lymphatic channels within the central stump have been undisturbed, the nerve has been rendered incapable of transmitting virus to the spinal cord by procedures which are known to produce a pronounced metabolic change in the cells of origin of the axones in the nerve, and thus necessarily in the axis-cylinders themselves.

Ten animals were used for this series of experiments. The results may be summarized as follows:

In four animals the right sciatic nerve was first frozen near the greater trochanter. Twice at 2–3 weeks' intervals the nerve was sectioned below the region of freeze, enough time being allowed for

regeneration of most of the fibers down to and below the point sectioned. The regeneration of fibers to this point was confirmed by biopsy and silver staining of a segment of nerve peripheral to the point of the section. Two to four weeks later, the sciatic nerve was sectioned again, above the point of the most proximal previous operation, and the central cut end of the nerve inoculated with potent virus suspension, according to the method described. None of these animals subsequently showed any sign of poliomyelitis.

In two animals the right sciatic nerve was sectioned at the mid-thigh level, and, at 2 weeks' intervals, sectioned twice again, each time at a distance of one centimeter above the previous point of section. Two weeks after the last of these three sections, the nerve was inoculated near the greater trochanter by the immersion method. One of the animals succumbed to poliomyelitis; the other animal remained well. The animal which developed poliomyelitis, however, showed sparing of most of the cells of the anterior horn which supply the inoculated sciatic nerve although all the other anterior horn cells of the lumbo-sacral cord were destroyed by the disease (figs. 4–6). This suggests that the induced resistance of the cells whose axones were sectioned was great, but not quite adequate in one case completely to protect the animal.

In three animals the right sciatic nerve was frozen with carbon dioxide ice near the greater trochanter, on three occasions separated by intervals of two weeks. Six weeks after the last freeze, the nerve was inoculated central to the point frozen, by the immersion method. Two of these animals succumbed to poliomyelitis after an incubation period of 4 days. The third animal remained well.

The right sciatic nerve of another animal was frozen near the greater trochanter thrice at two weeks' intervals, and after six weeks sectioned above the point of freeze. Twelve weeks later, there having been considerable regeneration of fibers, although the foot muscles were still inactive, the nerve was inoculated about 1 cm. above the point of previous sections, by the immersion method. The animal contracted poliomyelitis after 4 days.

Resumé of Series 5

These experiments demonstrate a remarkable phenomenon: in six of nine animals which thrice had had interruption of all of the fibers

in the sciatic nerve by freezing or cutting, at 2 to 4 weeks' intervals, the portion of the nerve central to the operative sites was rendered insusceptible to infection following inoculation with potent virus suspension. Presumably, a quantity of virus insufficient to produce infection, or perhaps no virus at all, could have been transmitted to the spinal cord by a morphologically intact sciatic nerve, although a method of inoculation was employed which invariably produces infection with the strain of virus used.

Of the first three animals in this series which became infected, two had had interruption of the sciatic nerve fibers by freezing rather than cutting. It has been found from other experiments (Howe and Bodian, '41) that axon interruption by freezing does not produce as severe retrograde cell change (chromatolysis) as does mechanical section, possibly because regeneration of the growing tip of the axons is easier across a frozen segment, and a less exuberant growth of collaterals occurs, than across a connective tissue scar. At any rate, the protection against invasion by the virus afforded the sciatic nerve by repetitive freezing operated in only one out of three cases, whereas in six out of seven cases with repetitive cutting, as well as freezing, complete protection resulted. Since the last animal in this series was inoculated three months after the last previous interruption of the nerve, it was to be expected that it would contract poliomyelitis, for at this time a considerable number of fibers in the nerve had completed their regeneration.

Two conclusions stand out clearly as a result of these experiments: 1) Repetitive interruption of the fibers in a nerve like the sciatic, by freezing and cutting at least thrice, prevents infection by inoculation of the nerve *central* to the points of interruption, *even when the virus is placed in direct contact with every nerve fiber*. Optimum intervals between successive interruptions of the fibers in the nerve, and the final inoculation, are between two and four weeks, that is, before any considerable number of fibers have completed their regeneration. 2) Since the nerve central to the points of interruption is morphologically intact as regards vascular supply, lymphatic connections, connective tissue sheaths, Schwann sheaths, and myelin sheaths, it must be concluded that it is the axis cylinder as well as the neurone of which it is a part (Howe and Bodian, '39 and '41), which is sufficiently altered by the successive distal injuries and the resulting regenerative efforts

to be rendered insusceptible to the virus. In other words, since central to the point of nerve section demonstrable changes are produced only in the neurone, it would appear that infection does not result because, from the initial point of contact, the virus is contained within the protoplasm of the refractory neurone. It is therefore highly probable that the axone protoplasm is the active transmitter of the virus in the nerve.

Series 6. Quantitative factors in intraneural inoculations

A definite quantitative factor was observed with respect to the number of nerve fibers exposed to the virus by the immersion method of inoculation. In three cases in which only the central cut end of the nerve to the hamstring muscles was inoculated, by immersion in virus suspension for two to three minutes, no poliomyelitis resulted. Inoculation of the central cut end of the cervical sympathetic trunk by the same method in two animals, using immersion times of 3 and 10 minutes respectively, failed also. Inoculation by immersion of a single lumbar anterior root, and a single lumbar posterior root, respectively, for three minutes, failed to produce infection.

In one case in which the central cut end of the vagus nerve (in the neck) was immersed in virus suspension for 3 minutes, poliomyelitis did not result, whereas in another animal in which the vagus nerve was similarly immersed for 15 minutes, neck paralysis, hoarseness and subsequent arm paralysis resulted after an incubation period of 17 days. Inoculation of the hypoglossal nerve near the hyoid bone by this method for 10 minutes was also successful in one case, the incubation period being 4 days. In all cases, control animals inoculated with the same virus suspension by the same method, but using the sciatic nerve, for 10 minutes contracted poliomyelitis after a period of 4–6 days.

These experiments point to the following factors as being quantitatively significant in infections by the intraneural route:

1. The numbers of nerve fibers exposed to virus and the length of time exposed. The failure of many nerves smaller than the sciatic nerve to transmit an infective dose when inoculated by the immersion method for a period of time adequate to produce infection by way of the sciatic nerve indicates that with a short time of immersion a rather large number of nerve fibers are necessary for transmission of an in-

fective dose. This fact further suggests that the virus does not multiply in the axons of the nerve cells but is passively transported within them, and this supposition tends to be confirmed by the fact that smaller nerves can transmit an infective dose if the immersion time in virus suspension is increased.

2. Nerve fiber size and fiber type. The successful inoculation of the hypoglossal nerve in the neck by the immersion method (10 minutes immersion-bulbar paralysis in 4 days) points to the ready susceptibility of a nerve predominantly composed of large, medullated, motor fibers, whereas the failure to infect by way of the cervical sympathetic trunk after an equivalent immersion time indicates that the fibers of finer caliber in sympathetic nerves are not especially susceptible. They could conceivably, nevertheless, transmit an infective dose if more fibers were involved and a greater period of time allowed for contact with virus. The vagus nerve, for example, composed of many more fibers, but also principally fibers of fine caliber, was found to transmit an infective dose after 15 minutes of immersion in virus suspension, but not after three minutes' immersion.

It is not possible to evaluate the relative potentialities of motor and sensory fibers for transmitting virus from the evidence here presented. There is little reason for not assuming however that both are capable of transmitting the virus. Pette ('30) has found after inoculation into the sciatic and median nerves that the first lesions appear in the posterior root ganglia, and concludes that the virus enters the spinal cord by way of the posterior roots. As additional evidence for the role of sensory fibers in the transmission of virus may be cited the successful inoculation by the intracutaneous route of some strains of poliomyelitis virus, and by analogy one could also cite the success of corneal inoculations of herpes virus in rabbits. However, the ready susceptibility of a predominantly motor nerve, such as the hypoglossal, suggests that the virus may be transmitted equally well along motor fibers.

DISCUSSION

The experimental evidence offered in the foregoing pages demonstrates the primacy of the axis-cylinder in the transmission of poliomyelitis virus in peripheral nerves, and renders highly dubious the

possibility that even minute quantities of virus can be transported to the central nervous system or within the latter *via* the so-called "perineural lymph-spaces," between the various sheaths of the axons, or within the Schwann cell chain. The mechanism of transport of the virus in the axis-cylinder remains a matter of speculation. The possibility of propagation by means of growth, introduced as early as 1887 by di Vestea and Zagari to explain neural spread of rabies virus, and favored by Goodpasture, '25, and others, although at first sight an entirely logical hypothesis, since the axon is after all only a process of the nerve cell, is weakened by the well-known low infectivity of white matter and nerve as compared with the gray matter of the nervous system. It is also possible that precisely those differences which do exist between perikaryon and axon, exemplified anatomically by the absence of nucleus and chromophil substance in the latter, may be more favorable for growth of virus in one and not in the other. We must add to this the fact that, by the method of inoculation employed in this work, a fairly large number of fibers must be exposed to the virus before infection occurs. This suggests that increase of the virus does not take place in the axon, but that the original amount which enters the axon must succeed in reaching the nerve cell body before multiplication and further spread can occur (see also Sabin, '37). It is possible that this may explain the fulminating effect of the virus in gray centers and the relatively minor direct pathological effect on fiber tracts (Bodian and Howe, '40b), as well as the absence of impaired conductivity in the axons before the cell bodies show injury (O'Leary, *et al.* '32). This would be especially true if the concentration of the virus in the axon is low. Such low concentrations undoubtedly may exist in the perikaryon as well, in certain cases, without marked pathological effect.

The possibility of passive transport of the virus in the axon has been doubted by O'Leary, *et al.* ('32) and by Cowdry ('34) who argue that the minute quantities that may gain access to the fiber would be largely adsorbed on the axon surfaces. This speculation denies, however, an equally likely supposition, namely that chemical substances, perhaps even of particle sizes comparable to those of the virus, may be normally transported from the perikaryon, and possibly the nucleus, along the axon (Gerard, '32). In fact, it is possible that instead

of being adsorbed on the surfaces, virus particles may move along fluid interstices or along interfaces in a gel at velocities greater than is possible by simple diffusion. Furthermore, Cowdry's assumption depends largely on the observations of de Renyi, '32, as to the gelatinous consistency of the axoplasm of the frog, but it is obvious that no critical evidence as to the normal consistency of mammalian axons exists at present. The studies of Speidel ('35) on living amphibian nerve fibers suggests that any form of irritation of axons produces swelling and the accumulation of fluid in the region of irritation. It might be speculated that local changes from a gel to sol state in the axon induced by the presence of the alien virus particles might permit translatory movements of the virus, assisted possibly by the deformation of the axoplasm resulting from stretching and constricting movements to which a nerve is normally subjected. In that case, transportation might be optimum in the largest fibers, which, as a matter of fact, seem to be more susceptible. Finally, the movement of virus particles even in a gel might be considerably influenced by the presence of surface charges. Until all of these factors have been evaluated experimentally it is useless to affirm or deny the possibility of active or passive virus movement, on the basis of inadequately determined migration velocities or of imperfectly understood physico-chemical properties of the axoplasm. In the last analysis, as is usually the case, the special problem of virus transport in nerves must await more fundamental studies of the properties of protoplasm, and particularly the special properties of nerve and virus protoplasm.

SUMMARY

1. When the sciatic nerve of the monkey is sectioned and the central cut end of the nerve moistened with potent MV virus suspension, poliomyelitis invariably results after an incubation period of between 4 and 6 days, and in one case as early as 3 days. This result is not altered by previous nerve section, or two nerve freezes, peripheral to the point of inoculation, two to six weeks previous to the inoculation (11 cases).

2. Inoculation of the sciatic nerve by the same method a few minutes after momentary freezing of the nerve at a point central to the inoculation fails to produce infection (4 cases). Since the freezing

causes degeneration of the nerve fibers peripheral to the point frozen, but does not interrupt the physical continuity of the nerve, it is clear that physical continuity of the nerve, in the absence of living nerve fibers, is not a sufficient condition for transmission of the virus along a nerve to the central nervous system.

3. If after freezing of the nerve at a single point, the nerve fibers are allowed to regenerate several centimeters into the peripheral segment, which is then transected and inoculated in the above-described manner, infection does not result unless regeneration has been allowed to proceed for at least 2 months before inoculation, or until a considerable number of nerve fibers have completed their regeneration. Apparently the regenerating portions of fibers in the course of regeneration, but which have not completed the process, are incapable of transmitting poliomyelitis virus to the central nervous system, at a time when the proximal parts of the same fibers in the central stump are susceptible. This refractoriness of the fibers in the peripheral stump may depend on their finer caliber, fewer numbers, or on other more obscure factors.

4. If successive interruption of the nerve fibers of the sciatic nerve is performed by transection or freezing, but preferably by transection, at 2–3 weeks' intervals, at least three times, the anatomically intact nerve fibers of the central stump as well as the incompletely regenerated fibers in the peripheral stump, are rendered incapable of transmitting virus to the central nervous system. When a considerable number of fibers have completed their regeneration, however, that is, after at least 2 months have elapsed following the last nerve fiber interruption, inoculation of the central stump results in poliomyelitis.

5. It is concluded that: a) The metabolic changes induced in neurones or their axons during the regenerative processes following repeated interruption of the axons by freezing and cutting at least thrice, prevents infection by inoculation of the nerve central to the points of interruption, *even when the virus of poliomyelitis is placed in direct contact with every axon.* Optimum intervals between successive interruptions of the fiber in the nerve, and the final inoculation, are between two and four weeks, that is, before any considerable number of fibers have completed their regeneration. b) Since the nerve central to the points of interruption is morphologically intact as regards

vascular supply, lymphatic connections, connective tissue sheaths, Schwann sheaths, and myelin sheaths, it appears that it is the axis cylinder, as well as the neurone of which it is a part, which is sufficiently altered in its metabolism by the successive distal injuries and the resulting regenerative efforts, to be rendered refractory to the virus. It is therefore highly probable that the axon protoplasm is the active transmitter of the virus in the nerve.

6. Evidence is presented which indicates that with the immersion method of inoculation of peripheral nerves an infective dose of virus can be transmitted to the central nervous system by a large number of fibers placed in contact with the virus for a few minutes, or by fewer fibers placed in contact with the virus for a longer period of time. This reciprocal relation between number of fibers and time of exposure to virus strongly suggests that the virus is not propagated in the nerve fiber by multiplying within it. The evidence does not support the view that sympathetic nerve fibers are especially susceptible to virus. The virus can probably reach the central nervous system by propagation along both motor fibers and sensory fibers.

7. The mechanism of transport of virus in the nerve is discussed.

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PLATE I

FIG. 1. Section of normal sciatic nerve of monkey, stained to show axis-cylinders. Note the numerous coarse fibers, and compare with figs. 2 and 3. Inoculation of such a normal nerve by the immersion method invariably results in poliomyelitis. 15 μ section. Protargol method. A121d-G-4. 210×.

FIG. 2. Section of right sciatic nerve of monkey, 4 cm. below a point frozen 6 weeks previously with CO_2 ice. Note the fine caliber of the regenerating fibers, as compared with the normal (fig. 1), or with fibers after 15 weeks regeneration (fig. 3). Inoculation of these regenerating nerve fibers at this point by the immersion method failed to produce poliomyelitis. 15 μ section. Protargol method. A78-68. 210×.

FIG. 3. Section of right sciatic nerve of monkey, ca. 10 cm. below a point frozen with CO_2 ice 15 weeks previously. Note the far advanced state of regeneration of the fibers, associated with considerable functional recovery in the leg, and the numerous coarse fibers. At this point, inoculation of the regenerating portion of the nerve by the immersion method resulted in typical poliomyelitis, without sparing of the cells of origin of the inoculated, regenerated fibers. 15 μ section. Protargol method. A70a-9. 210×.

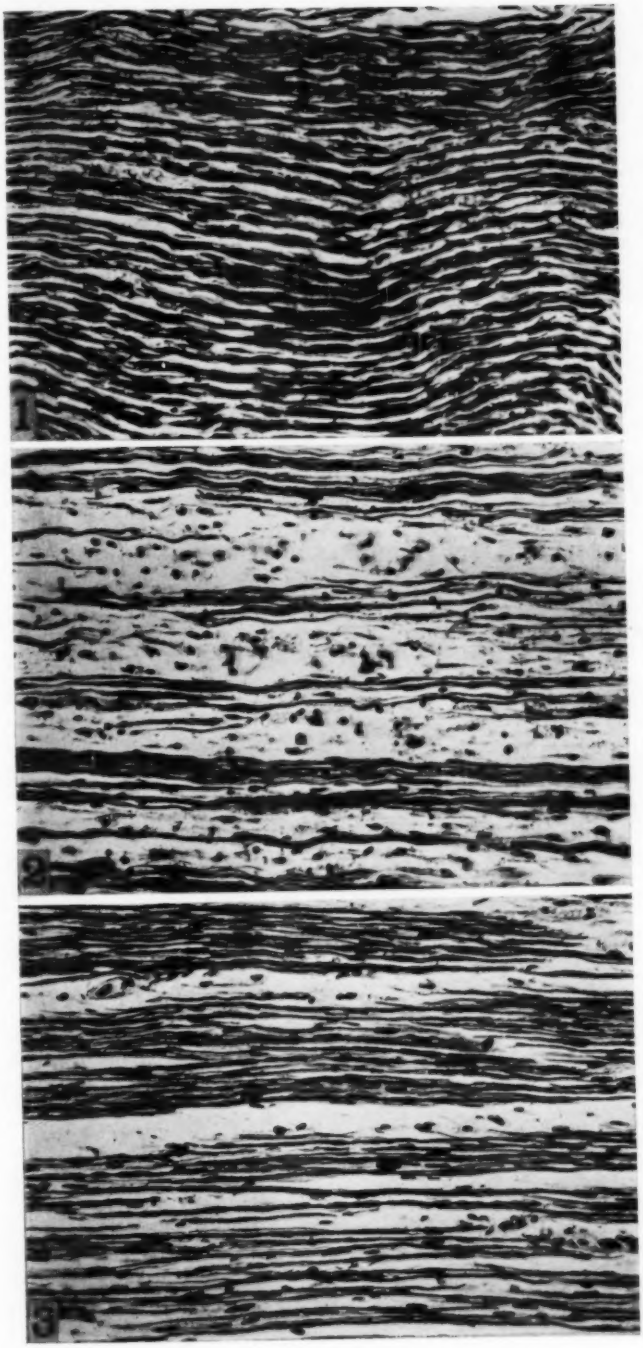
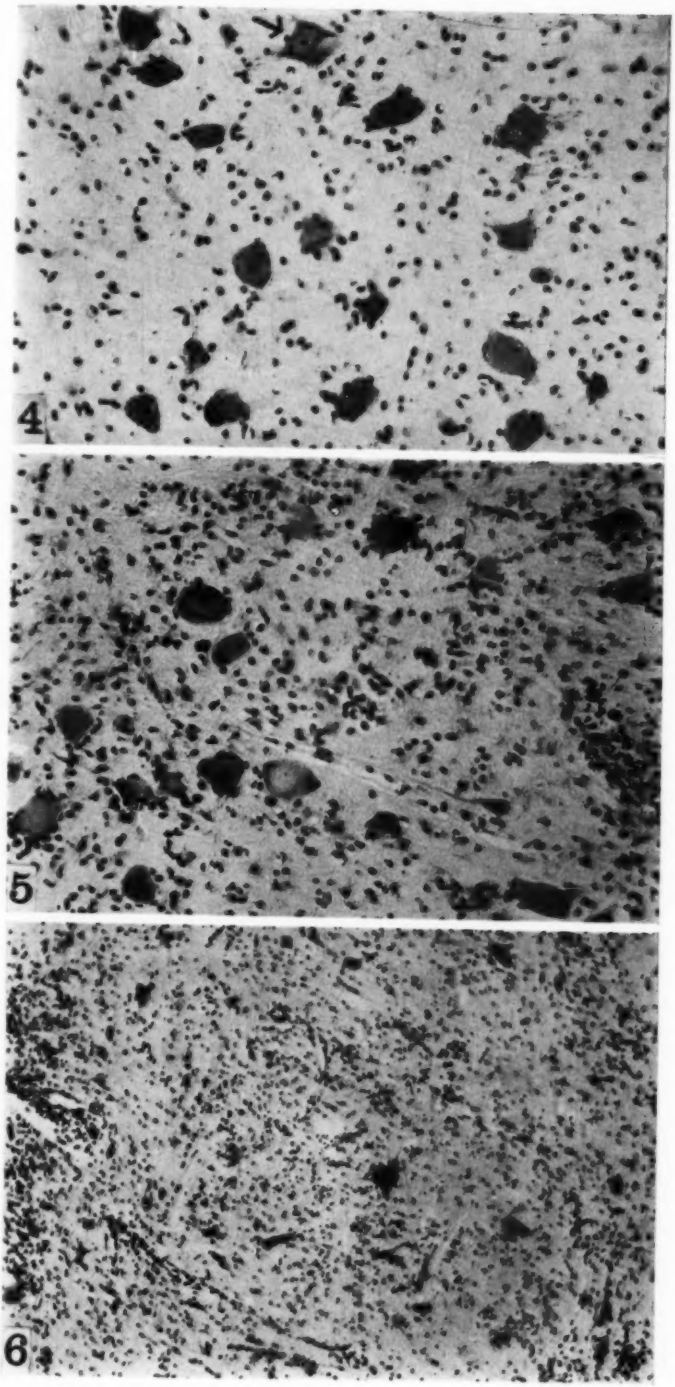

1
2
3

PLATE II

FIG. 4. Section of lumbar cord (L_6), showing right anterior horn. Right sciatic nerve had been first frozen, and then sectioned twice at points 2 and 1 cm. below the frozen region, at 2–3 weeks intervals, at which time the fibers had regenerated to a point below the site of section. Three weeks following the last section, the nerve was inoculated by the immersion method above the frozen area, but no poliomyelitis resulted. The animal was killed seventeen days after the inoculation. The section illustrates the uniformity of chromatolysis resulting after successive injuries to the nerve fibers of the sciatic nerve. The border cell indicated by the arrow does not belong to the sciatic nerve group, and shows no axon reaction. The chromatolysed cells are to be compared with this cell, and with the virus-refractory cells in fig. 5. 10 μ section. Gallocyanin stain. A122-15. 160×.

FIG. 5. Right anterior horn of lumbar cord (L_6) of animal treated as in case shown in fig. 4, but which succumbed to poliomyelitis 6 days after inoculation; three other animals similarly treated remained well. The cells shown are those associated with the operated sciatic nerve. They show chromatolysis to a degree similar to that apparent in fig. 4, and have been largely spared by the poliomyelitic process. Cell at extreme right is undergoing neuronophagia. 10 μ section. Gallocyanin stain. A120-22. 160×.

FIG. 6. Left anterior horn of section shown in fig. 5. The cells on this side (unoperated) have been largely destroyed by the poliomyelitic process. Cells which are visible, such as the one shown in the center, are either seriously vacuolized or undergoing neuronophagia.



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DURATION OF INFECTIVITY OF TREPONEMA PALLIDUM IN CITRATED BLOOD STORED UNDER CONDITIONS OBTAINING IN BLOOD BANKS[1]

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The transfer of whole blood from one person to another by the immediate indirect method carries with it the potential risk of transmitting syphilitic infection. This danger is certainly reduced to a minimum by careful selection and examination of donors, and actually relatively few instances of transfusion syphilis have been reported.

In recent papers on the subject Morgan (1) reviewed 16 cases of indubitable transfusion syphilis, Salkind (2) 39 cases, Klauder and Butterworth (3) 35 cases, and Eichenlaub and Stolar (4) 41 cases. Since the paper by the last named authors was submitted for publication 7 additional cases have been recorded (5, 6, 7, 8, 9, 10). Among the total reported cases, in at least 10 instances blood was transfused from a donor who was in the incubation period of the disease, *i.e.*, before the appearance of a primary lesion or the development of a positive serologic test, and in at least 9 other instances the donor was in the sero-negative phase of the primary stage of syphilis. Another patient was infected by a donor who had recently been treated for early syphilis and who at the time of transfusion had a negative serologic test. In these 20 transfusions routine serologic examination of the donor's blood therefore did not disclose the presence of the infection. It is to be supposed that many similar instances of transfusion syphilis have gone unrecognized or unreported.

In the past few years stored blood has been used to an increasing

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extent for transfusions, and blood banks are maintained in many of the larger hospitals. This subject has been recently reviewed by Ham (11). Citrated blood may be transfused with impunity after storage of 14 days, although reactions seem to be more common if the blood has been refrigerated for longer than 8 to 10 days. In one large hospital the average duration of storage has been about 4 days (12).

It is known that *Treponema pallidum* does not survive *in vitro* at ordinary temperatures for many days, and it is probable that the use of stored blood for transfusion further reduces the risk of transfusion syphilis. The experiments reported in this paper were designed to obtain information on the probable limits of safety in using such blood even though it be taken from a syphilitic donor. *Treponema pallidum* was added to citrated blood from both human beings and rabbits, and the infectivity of the mixture for rabbits determined after various periods of refrigeration. Blood from syphilitic rabbits known to be in an infectious stage was likewise tested. Blood from human beings with early syphilis was not tested because even under the most favorable conditions rabbits are infected with difficulty with such material. The results obtained with a strain of *T. pallidum* well adapted to the rabbit were regarded as being a more reliable index of survival or death of the organism than would be the results obtained with freshly isolated strains.

EXPERIMENTAL METHOD AND RESULTS

Citrated blood to which T. pallidum had been added

Blood for storage was prepared according to the method used in the blood bank of the Johns Hopkins Hospital (12). Freshly drawn blood was diluted with 5 per cent sodium citrate in the proportion of 5 cc. of sodium citrate to 50 cc. of whole blood. No dextrose was added. To nine parts of the citrated blood, either human or rabbit, was added one part of a tissue emulsion rich in *T. pallidum*. This spirochete emulsion was prepared by emulsifying a syphiloma of the rabbit's testis in infusion broth. After centrifugation, the supernatant fluid was free of gross tissue particles and contained 3 to 4 actively motile treponemes per oil immersion field. The Nichols strain of *T. pallidum* was used throughout. After the citrated blood

and spirochete emulsion were thoroughly mixed, the suspension was distributed in 2 cc. vials. The vials were stoppered and stored in the refrigerator at a temperature of approximately 2°C.

In order to test the infectivity of the mixture, normal rabbits were inoculated in one testis with 0.5 cc. amounts before the blood was refrigerated and at various intervals after refrigeration. In some experiments, animals inoculated intratesticularly with refrigerated blood were also inoculated intracutaneously at three sites on the back with 0.1 cc. of the same specimen. All animals were examined at least twice weekly for evidences of syphilitic infection. If a lesion developed, it was designated as "positive" only when *T. pallidum* was demonstrated by darkfield examination. Parenthetically, it might be noted that all lesions suggestive of syphilis proved to be darkfield positive. Rabbits in which no suspicious lesion developed either in the testis or on the back were designated as "negative," and were observed for a minimum period of 90 days unless death of the animal supervened. In the case of animals remaining negative for 90 days, the popliteal lymph nodes were removed, emulsified in a small amount of broth, and the emulsion inoculated into one testis of each of two normal rabbits. These rabbits in turn were observed for 90 days for evidences of syphilitic infection. When two animals which had been inoculated with the same specimen of stored blood, survived the ninety-day period of observation, their popliteal nodes were pooled for transfer to the pair of normal rabbits.

T. pallidum in citrated human blood

In order to test the probable range in point of time of the infectivity of *T. pallidum* in human blood, a preliminary experiment was made in which specimens of human blood-spirochete mixtures were inoculated at intervals of 3, 7, 10, and 14 days, respectively. As controls one sample of the same mixture was inoculated immediately before storage. The results are shown in Table I.

Both rabbits inoculated with blood samples before storage developed typical syphilitic lesions of the testis within the usual incubation period of the experimental disease. None of the animals inoculated with samples that had been refrigerated for 3 days or longer developed a lesion, and in each instance their popliteal lymph nodes failed to produce lesions when inoculated into the testes of normal rabbits.

In Table II are shown the results of the inoculation of another mixture of human blood and *T. pallidum* before storage, and at intervals of 12, 24, 48, 72, 96, 120, and 144 hours after storage. In this experiment the same specimen was inoculated both intratesticularly and intracutaneously in the same rabbit. It will be noted that both animals inoculated with specimens before storage developed testicu-

TABLE I

Infectivity for Rabbits of Treponema pallidum in Citrated Human Blood Stored for Various Periods at Refrigerator Temperature

Inoculum—9 parts citrated human blood plus 1 part spirochete emulsion

Rabbit 7-91

DURATION OF STORAGE OF BLOOD-SPIROCHETE MIXTURE AT TIME OF INOCULATION	RABBIT INOCULATED, NUMBER	RESULT OF INTRATESTICULAR INOCULATION		RESULT OF LYMPH NODE TRANSFERS AFTER 90 DAYS		
		Incubation period	Duration of observation	Rabbit inoculated, number	Result of intratesticular inoculation	Duration of observation
			days			*days*
Inoculated immediately	8-19	Pos.* 22 days	—	Not made	—	—
	8-20	Pos. 25 days	—	Not made	—	—
3 days	8-25	Negative	92	9-54	Negative	106
				9-55	Negative	106
7 days	8-39	Negative	92	9-59	Died	12
				9-60	Negative	102
10 days	8-45	Negative	92	9-65	Negative	99
				9-66	Negative	99
14 days	8-46	Negative	97	9-73	Died	12
				9-74	Negative	90

* Positive indicates the development of a characteristic intratesticular or intracutaneous lesion that was darkfield positive for *Treponema pallidum*.

lar and cutaneous lesions within the usual incubation period. Specimens inoculated 12 and 24 hours after storage likewise gave rise to typical syphilitic lesions, but the incubation periods tended to be longer than in the controls. One animal inoculated with a 24-hour specimen failed to develop lesions at the sites of intracutaneous inoculation. Rabbits inoculated with specimens of the same blood-spirochete mixture after storage for 48 hours and longer failed to

develop syphilitic lesions and the non-infectivity of their lymph nodes indicates that they were not infected by the organisms in the refrigerated mixtures.

TABLE II

Infectivity for Rabbits of Treponema pallidum in Citrated Human Blood Stored for Various Periods at Refrigerator Temperature

Inoculum—9 parts citrated human blood plus 1 part spirochete emulsion

Rabbit 8-73

DURATION OF STORAGE OF BLOOD-SPIROCHETE MIXTURE AT TIME OF INOCULATION	RABBIT INOCULATED, NUMBER	RESULT OF INOCULATION			RESULT OF LYMPH NODE TRANSFERS AFTER 90 DAYS		
		Intratesticular and incubation period	Intracutaneous back and incubation period	Duration of observation	Rabbit inoculated, number	Result of intratesticular inoculation	Duration of observation
				days			*days*
Inoculated immediately	9-02	Pos. 22 days	Pos. 16 days	—	Not made	—	—
	9-05	Pos. 16 days	Pos. 14 days	—	Not made	—	—
12 hours	9-08	Pos. 27 days	Pos. 14 days	—	Not made	—	—
	9-09	Pos. 32 days	Pos. 25 days	—	Not made	—	—
24 hours	9-12	Pos. 35 days	Negative	—	Not made	—	—
	9-13	Pos. 38 days	Pos. 35 days	—	Not made	—	—
48 hours	9-16	Negative	Negative	94	10-05	Negative	92
	9-17	Negative	Negative	94	10-06	Negative	92
72 hours	9-20	Died 21 days	—	—	—	—	—
	9-21	Negative	Negative	93	10-07	Negative	92
					10-08	Died	19
96 hours	9-28	Negative	Negative	92	10-11	Negative	92
	9-29	Negative	Negative	92	10-12	Negative	92
120 hours	9-32	Died 21 days	—	—	—	—	—
	9-33	Negative	Negative	92	10-15	Negative	91
					10-16	Negative	91
144 hours	9-36	Negative	Negative	91	10-19	Negative	91
	9-37	Negative	Negative	91	10-20	Negative	91

T. pallidum in citrated rabbit blood

Since the strain of *T. pallidum* employed in these experiments had been propagated for many years in rabbits, it was thought that per-

haps rabbits' blood might provide a more favorable medium for the survival of these organisms than would human blood. An experiment similar to the previous one was made, except that the *T. pallidum* emulsion was added to citrated rabbit blood instead of to human blood. The method of preparation of the blood and the spirochete emulsion was the same in each instance. The mixture was refrigerated in the same manner and inoculations were made before refrigeration and at the same intervals after the beginning of refrigeration, namely at 12, 24, 48, 72, 96, 120, and 144 hours. Inoculations were made both in the testis and intracutaneously on the back.

The results of this experiment are shown in Table III. One surviving rabbit inoculated with the blood-spirochete mixture before refrigeration showed typical syphilitic lesions after a relatively short incubation period. Animals inoculated at 12, 24 and 48 hours were likewise positive, but the incubation periods in the 48-hour rabbits were definitely prolonged and, in contrast to rabbits inoculated earlier, no lesions developed at the sites of intracutaneous inoculation. Animals inoculated at 72 hours and later failed to develop lesions and their popliteal lymph nodes did not give rise to lesions in normal rabbits. These results indicate that the potency of the inoculum was materially reduced after a storage period of 48 hours, and that at 72 hours the mixture was no longer infectious for rabbits.

In an experiment somewhat similar to the one just reported, Bloch (13) found that a rabbit blood-spirochete mixture which had been stored under blood bank conditions was infectious for rabbits after 24, 48, and 72 hours, but not at 96 hours. As in our experiments the incubation period of the lesions produced by the refrigerated mixtures were significantly longer than were those arising from the inoculation of the mixture before storage. The blood-spirochete mixture employed by this investigator apparently contained many more *T. pallidum* than did our mixture, and this may have accounted for the slight difference in results.

Naturally infected rabbit blood

The procedures in this experiment differed somewhat from those in the foregoing experiments. In an effort more closely to simulate the conditions obtaining in the transfusion of human beings, blood was

drawn from rabbits with extensive active syphilitic lesions, citrated, and stored at refrigerator temperature and, after an appropriate interval, injected intravenously into normal rabbits.

TABLE III

Infectivity for Rabbits of Treponema pallidum in Citrated Rabbit Blood Stored for Various Periods at Refrigerator Temperature

Inoculum—9 parts citrated rabbit blood plus 1 part spirochete emulsion

Rabbit 8-73

Duration of storage of blood-spirochete mixture at time of inoculation	Rabbit inoculated, number	Result of inoculation			Result of lymph node transfers after 90 days		
		Intratesticular and incubation period	Intracutaneous back and incubation period	Duration of observation	Rabbit inoculated, number	Result of intratesticular inoculation	Duration of observation
				days			*days*
Inoculated immediately	9-03	Pos. 18 days	Pos. 12 days	—	Not made	—	—
	9-04	Died 14 days	—	—	Not made	—	—
12 hours	9-10	Pos. 29 days	Pos. 20 days	—	Not made	—	—
	9-11	Pos. 22 days	Pos. 18 days	—	Not made	—	—
24 hours	9-14	Pos. 28 days	Pos. 24 days	—	Not made	—	—
	9-15	Died 15 days	—	—	Not made	—	—
48 hours	9-18	Pos. 41 days	Negative	—	Not made	—	—
	9-19	Pos. 39 days	Negative	—	Not made	—	—
72 hours	9-22	Died 27 days	—	—	—	—	—
	9-23	Negative	Negative	93	10-09	Negative	92
					10-10	Negative	92
96 hours	9-30	Died 10 days	—	—	—	—	—
					10-13	Negative	91
	9-31	Negative	Negative	93	10-14	Died	57
120 hours	9-34	Negative	Negative	92	10-17	Negative	91
	9-35	Negative	Negative	92	10-18	Negative	91
144 hours	9-38	Negative	Negative	91	10-21	Negative	91
	9-39	Negative	Negative	91	10-22	Negative	91

Rabbits serving as the source of the infected blood had been inoculated intratesticularly with the Nichols strain of *T. pallidum*, and at the time blood was withdrawn, exhibited a well developed syphilitic

orchitis of a few days' duration. On the basis of previous experience, it was assumed that this blood was infectious. This assumption proved to be correct as shown by the results of immediate inoculation of normal animals.

Approximately 40 cc. of blood was withdrawn by cardiac puncture from each source rabbit. To this blood was added a 5 per cent sodium citrate solution in the proportion of 5 cc. of the solution to 50 cc. of whole blood. Five-tenths cc. of the citrated blood was inoculated immediately into one testis of one or two normal rabbits. The citrated blood was immediately placed in the refrigerator at a temperature of about 2°C. After 48, 72, or 96 hours the citrated blood was injected into one normal rabbit, 0.5 cc. being inoculated into one testis, and the remaining amount, usually 35–45 cc., intravenously. Altogether the test rabbit received 70 to 80 times the dose of the control animal inoculated immediately after withdrawal of the blood. The animals to which stored blood was given intravenously exhibited no obvious clinical reaction to the transfusion. The transfused animals were examined twice weekly for generalized lesions of the skin, bones or eyes, as well as for testicular lesions.

The results of these experiments are shown in Table IV. In each instance the control animal developed syphilitic lesions, thus proving the infectivity of the freshly drawn citrated blood. The incubation period of the disease in the control animals tended to be longer when naturally infected blood was inoculated than when blood to which treponemes had been added was used. It is probable that *T. pallidum* was present in much smaller numbers in the former inocula. None of the animals transfused with citrated blood stored for 48, 72, and 96 hours developed lesions despite the large amount of potentially infected blood injected. Popliteal nodes removed from these animals 90 days after transfusion failed to produce lesions upon intratesticular inoculation of normal rabbits.

Since the number of samples of blood tested in these experiments is small, the results serve only to confirm the findings of the preceding experiments. They do indicate, however, that syphilis spirochetes present in blood during the course of the experimental disease in rabbits do not possess any unusual capacity to survive longer than those added to blood artificially.

TABLE IV

Infectivity of Citrated Whole Blood from Syphilitic Rabbits after Storage at Refrigerator Temperature for Varying Periods of Time

SOURCE OF BLOOD, RABBIT NUMBER	DURATION OF STORAGE AT TIME OF INOCULATION	RABBIT INOCULATED, NUMBER	ROUTE OF INOCULATION AND AMOUNT OF BLOOD INOCULATED*	RESULTS OF INOCULATION AND INCUBATION PERIOD	DURATION OF OBSERVATION	LYMPH NODE TRANSFER AFTER 90 DAYS		
						Rabbit inoculated, number	Results of inoculation	Duration of observation
					days			*days*
8-19	Inoculated immediately	8-55	I.T. 0.5 cc.	Pos. 41 days	—	Not made	—	—
	48 hours	8-56	I.T. 0.5 cc. I.V. 40 cc.	Negative	90	9-75 9-76	Negative Negative	97 97
9-62	Inoculated immediately	9-79 9-80	I.T. 0.5 cc. I.T. 0.5 cc.	Pos. 20 days Pos. 41 days	— —	Not made Not made	— —	— —
	72 hours	9-83	I.T. 0.5 cc. I.V. 43 cc.	Negative	94	10-64 10-65	Negative Negative	90 90
9-64	Inoculated immediately	9-82	I.T. 0.5 cc.	Pos. 41 days	—	Not made	—	—
	96 hours	9-90	I.T. 0.5 cc. I.V. 35 cc.	Negative	93	10-66 10-67	Negative Negative	90 90
8-20	Inoculated immediately	8-69	I.T. 0.5 cc.	Pos. 44 days	—	Not made	—	—
	96 hours	8-71	I.T. 0.5 cc. I.V. 40 cc.	Negative	90	9-77 9-78	Negative Negative	97 97

* I.T., intratesticularly, I.V., intravenously.

DISCUSSION

The experiments reported above indicate that, under the conditions obtaining in blood banks, syphilis spirochetes probably undergo progressive deterioration during the storage period. Even when large numbers of virulent treponemes were added to citrated whole blood the mixtures were not infectious for normal rabbits after storage for three days or longer. After storage periods of one and two days, although viable organisms were still present, they were evidently considerably reduced in numbers or in virulence, since the incubation period of the lesions resulting from the inoculation of the same amounts of the stored mixture was significantly prolonged, and in some instances, the inoculated animals escaped infection. As noted above, Bloch (13) in one experiment obtained infection with material stored for 72 hours. Nevertheless, the results of the two studies are in substantial agreement, and indicate that the infectivity of syphilis treponemes in citrated whole blood rarely persists for longer than three days at refrigerator temperature.

In our experiments, and those of Bloch in which *T. pallidum* was added to citrated whole blood, treponemes were present in much larger numbers than is the case in blood from human beings with syphilis. Blood from naturally infected rabbits failed to give rise to syphilitic infection after 48, 72, and 96 hours in the few instances tested. It seems fair to conclude that citrated whole blood stored for four days or longer, even though obtained from a donor with active early syphilis, can probably not transmit syphilitic infection.

SUMMARY

1. Virulent *Treponema pallidum* added to citrated whole human blood stored under conditions obtaining in blood banks failed to give rise to infection in normal rabbits after storage periods of 48 hours or longer.

2. Virulent treponemes added to citrated whole rabbit blood and similarly stored was infectious for normal rabbits after 48 hours' storage but not after 72 hours or longer. In a similar experiment by Bloch infection was obtained after a storage period of 72 hours.

3. In a few instances normal rabbits were not infected when transfused with naturally infected rabbit blood which had been stored for 48, 72 or 96 hours.

CONCLUSIONS

Under conditions obtaining in blood banks, *Treponema pallidum* undergoes progressive deterioration in citrated whole blood during the storage period. There is a corresponding reduction in the risk of transmitting syphilis by transfusion, and it is probable that blood stored for 4 days or longer can no longer transmit this disease.

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PROCEEDINGS OF THE MEETING OF THE JOHNS HOPKINS MEDICAL SOCIETY

Held in the Hurd Memorial Hall, January 13, 1941

The President of the Society, Dr. Warfield M. Firor, presided. Abstracts of the papers and discussions follow:

Case Presentation: Resection of Head of Pancreas for Carcinoma. I. R. Trimble and J. W. Parsons. (Departments of Surgery and Medicine.)

The report was presented of a woman of forty-two years who had obstructive jaundice. At operation on April 26, 1940, a papillary growth was found in the second portion of the duodenum surrounding the ampulla of Vater, which was proven, by examination of a frozen section, to be adenocarcinoma. The first three portions of the duodenum, the distal stumps of the common and pancreatic ducts and a small portion of the head of the pancreas, and the pyloric end of the stomach were resected. The gastro-intestinal tract was restored with an anterior Polya gastro-enterostomy. The stump of the common duct was transplanted into the distal loop of jejunum of this enterostomy. The pancreatic stump together with its ducts was closed with interrupted mattress stitches of chromic catgut. No attempt was made to reconnect the pancreatic ducts with the intestine. The gallbladder was drained to remove the pressure from the choledocho-enterostomy.

The patient recovered rapidly from operation without the formation of a duodenal or a biliary fistula. She has remained well until the present time, eleven months since operation, and is back at work. The deprivation of the external secretion of the pancreas has had no apparent effect upon the digestion of fat, carbohydrate, or protein in this patient.

Management of Thyroid Disease. Frank H. Lahey. (The Lahey Clinic, Boston, Massachusetts.)

Dr. Lahey discussed some of the high-lights of thyroid surgery as encountered in his very large experience. He reported that the operative mortality was less than 1 per cent in over 18,000 cases subjected to thyroid operations by himself and his associates. He advocated radical resection for carcinoma of the thyroid, and said that he believed that all adenomata of the thyroid should be removed, owing to the likelihood of development of malignant changes. This applied especially in the case of aberrant thyroid masses. In certain cases of hyperthyroidism in which the status of the patient is difficult to evaluate, studies of the blood iodine level seem to give more valuable information than is obtained by estimations of the basal metabolic rate.

Dr. Lahey stressed the fact that true substernal adenomata which are too large to be removed *in toto* without dividing bone, may be removed successfully by morcellation.

Illustrative lantern slides were shown.

Aspects of Aviation Medicine. J. F. FULTON, M.D. (*Laboratory of Physiology, Yale University School of Medicine.*)

After drawing attention to the fact that Robert Boyle was the first to conduct physiological studies on respiration in a decompression chamber and that through these studies he had recognized the phenomenon of air embolism (*Philos. Trans.*, 1670, **5**: 2044) the three principle problems encountered in modern high combat flying were discussed: (i) the bends; (ii) anoxia; (iii) effects of acceleration.

Such rapid ascent is now possible in modern combat aircraft (a fighter plane may ascend at nearly a mile a minute) that the pilot may experience symptoms similar to those well-known as the bends among divers and caisson workers. It was mentioned that previous inhalation of oxygen prior to ascent and slower rate of ascent may diminish or prevent the bends syndrome. It is believed due, as with caisson disease, to the liberation of nitrogen in the soft tissues of the body, and when liberated in the blood stream in sufficient quantities, air embolism may result.

Under anoxia Dr. Fulton discussed the various series of anoxia in relation to respiration, mentioning that some authors believe gradual diminution of oxygen partial pressure resulted in alkalosis of the blood, whereas others believe that it leads to an acidosis. Recent experimental studies bearing on the problem were briefly mentioned.

The effect of acceleration came first to be reckoned with as a serious problem in 1928 at the Schneider Cup Races when, owing to rapid turns, pilots lost consciousness owing to centrifugalization of blood away from the head. The same difficulties are encountered in dive bombing operations and in close turns during combat. The need for some mechanical means of preventing the flow of blood from the head was stressed and several possible solutions of the problems found in the current literature were mentioned.

DISCUSSION

Dr. Leslie N. Gay asked Dr. Fulton whether helium had ever been tried in these combat planes?

Dr. Fulton said that helium had made possible the rescue of all living passengers on the Squalus. Its use in combat flying may be possible because nitrogen, under low pressure, has properties which helium does not possess. It is possible that helium, if used over several hours, could throw off body nitrogen. Dr. Fulton said that only certain aspects of helium are known but he felt that it might be useful. For various technical reasons helium has not been tried on a large scale so far.

Dr. Philip Bard said that it has been shown that when oxygen is administered to human beings at an altitude of 30,000 feet they collapse. He wondered if the administration of oxygen to animals at their ceiling height had been tried.

Dr. Fulton replied that when oxygen is given to animals at their ceiling, their pH falls and goes considerably below the existing pH and the animals collapse. He said that it was very dangerous to give ordinary animals pure oxygen. There are various instances of collapse in human beings who have been given oxygen at ceiling height.

BOOK REVIEWS

(These reviews represent the individual opinions of the reviewers and not necessarily those of the members of the Editorial Board of this Journal.)

Bird Malaria. By REDGINAL HEWITT. 228 pp. Illus. $1.10. *The Johns Hopkins Press, Baltimore, 1940.* (American Journal of Hygiene Monographic Series, No. 15, July, 1940.)

This is a complete review of the work of authors throughout the world since the discovery by Laveran, in 1880, of the human malarial parasite and that of Danilewsky, in 1885, of similar parasites in birds. It could not be more carefully arranged to give a clear presentation of present knowledge of the whole subject, especially as illustrated by bird malaria, with an outline of the problems which still remain, such as questions of immunity, the nature of exoerythrocytic forms, and the immediate invasion of sporozoites after their introduction by the bite of the infecting mosquito.

Methods of study are described in detail and the extraordinary results of the work of recent years in recognizing a great many new species of bird malaria parasites are given with a key to species identification. No mention is made of the forms of the parasites which infect other animals than birds. The stages in the life history of the parasite, the effects produced in the organs of the host and the various evidences of immunity with the attempts toward neutralization of the infection by the action of drugs, make up much of the book which ends with a long series of problems suggested for investigation, and a complete bibliography of bird malaria.

W. G. M.

Text-Book of Ophthalmology. By SIR W. STEWART DUKE-ELDER. Vol. III. *Diseases of the Inner Eye.* 1373 pp. Illus. $18.50. *C. V. Mosby Company, St. Louis, 1941.*

In his third volume Sir Stewart Duke-Elder has maintained the high standards of the preceding volumes. This simple statement of fact makes it superfluous to write a lengthy review for we have learned that the first two volumes are essential in the practice of our specialty. The third volume unquestionably deserves its place beside the other two.

The third volume is concerned with diseases of the inner eye, and contains sections which deal with the uveal tract, the retina, optic nerves, lens, vitreous body, glaucoma and intraocular parasites. In its general arrangement it is similar to the earlier volumes. There is not quite the same wealth of detail but such would not have been possible in a single volume. In its 1400 pages the

material has been well chosen and has been condensed to an astonishing degree, but never to the point of interfering with clarity of expression or fine descriptive writing. From the standpoint of presentation of clinical material the author constantly leaves the reader with definite knowledge as to what is fact and what is surmise. Certainly in this regard this volume and its earlier companions stand second to no other work on the subject.

The wealth of well chosen illustrations is one of the special features of the volume; with the exception of a few they are very fine. As in previous volumes the printing, by the C. V. Mosby Company, is praiseworthy. The bibliographies are extensive and the method of appending a full list of references at the end of each section is admirable.

English ophthalmologists have every right to feel proud of Duke-Elder's volume, published during such difficult times in England. Certainly American ophthalmologists will be anxious to congratulate him.

F. B. W.

Medical Vocabulary—English, German, French, Italian, Spanish. By JOSEPH S. F. MARIE. 358 pp. $3.00. *P. Blakiston's Son & Co., Philadelphia, 1939.*

This vocabulary, in which English medical terms are arranged alphabetically, gives the German, French, Italian, and Spanish equivalents on the same line. Some remarks on the pronunciation of foreign words and a short dictionary of medical phrases end the book. As a whole it should be used with some caution, and no reliance whatsoever should be placed on the German column (supplied by Dr. Milton K. Meyers as the preface states). This abounds in grave mistakes and downright wrong translations. For instance: anatomist is Anatom, not "Anatomiker"; "vergehen" for (to) faint is quite impossible and so is "Gedärm" for garbage, for it means intestines. As to German genders, the book plays havoc with them. "Blut" (blood) is indicated as masculine, and "Knochen" (bone) as neuter.

O. T.

Psychotherapy. By LEWELLYS F. BARKER. 218 pp. $2.00. *D. Appleton-Century Co., New York and London, 1940.*

This little book of 200 pages presents in a clear, compact, readable form a discussion of psychotherapy. There is probably no word in medical parlance used so freely and loosely by physicians and laymen as the word "psychotherapy." It is a large umbrella covering all sorts of scientific and quasi-scientific attempts "to improve the condition of a human being by means of influences that are brought to bear upon his mind (psyche)." These approaches embrace the commonsense understanding of the good family doctor, the treatment of social, personality and organic factors based on comprehensive diagnostic studies of modern psychiatry, the techniques of the various schools of psychoanalysis, and the patter and rituals embodied in magic and quackery of various kinds. Dr. Barker classifies these approaches in an attempt to bring order out of chaos, and to clarify

and evaluate their contributions for the busy medical reader in a fair and dispassionate manner. He points out the fact that "many physicians are so markedly repelled by the language and the ideas of some of the writers on psychotherapy (especially on psychoanalysis) that they feel that a subject so apparently recondite can be of but little value in ordinary medical practice and can be safely ignored. . . . There is danger that even the simpler and more easily applied methods of psychotherapy may be thrown overboard along with the recondite by some physicians to the great detriment of patients who need psychotherapy in addition to other forms of treatment." A glossary and well selected bibliography increases the practical value of this book to the general practitioner and specialist.

E. L. R.

Lipidoses: Diseases of the Cellular Lipid Metabolism. By SIEGFRIED J. THANNHAUSER. Edited by HENRY A. CHRISTIAN. (Reprinted from Oxford Loose-Leaf Medicine.) 370 pp. Illus. $6.00. *Oxford University Press, New York [etc.], 1940.*

In a most lucid manner the author discusses our present knowledge of the physiology and chemistry of the lipids and the mechanisms responsible for hyperlipemia, and then proceeds to consider in detail the clinical disorders of lipid metabolism—the primary forms of xanthomatosis, the secondary xanthomatoses due to hyperlipemia of various kinds, localized xanthoma formation, Gaucher's disease and Niemann-Pick disease. The clinical syndromes and the underlying pathology are described and illustrated in great detail and the presentation of the many chemical studies undertaken in the attempt to throw light on these disorders is well done. In contrast to the secondary xanthomatoses, which are due to hyperlipemia—idiopathic or caused by diabetes, nephrosis, von Gierke's disease or pancreatitis—the author maintains that the primary lipidoses represent a metabolic disorder of the cells in which the abnormal lipids accumulate. These primary disorders cannot be influenced by dietary therapy and should not be subjected to dietary restrictions.

This volume, unique in its completeness and written by the outstanding student of this group of obscure diseases, is well worth a careful study and will be welcomed by all.

L. E. H., JR.

Foreign Bodies Left in the Abdomen. By HARRY STURGEON CROSSEN and DAVID FREDERIC CROSSEN. 762 pp. Illus. $10.00. *C. V. Mosby Company, St. Louis, 1940.*

In the pursuit of a most stimulating hobby, Dr. Harry S. Crossen has for many years gamely stalked the perils of the forgotten foreign body left in the abdomen. In 1907 he published his first critique on the dangers of the detached sponge and suggested an original and most ingenious improvement, the continuous sponge.

This method of sponge control is indeed a commendable remedy as it piths the very core of the problem by automatically eliminating the individual pad.

The present book is a thorough and replete study of all foreign bodies left in the abdominal cavity and is divided into two distinct parts—one treating the subject from a surgical standpoint and written by Harry S. Crossen, M.D., and the other from a legal standpoint and written by David F. Crossen, LL.B.

The work was "undertaken to emphasize to surgeons the danger of occurrence of the serious accident of leaving a foreign body in the abdominal cavity, to work out the best plan of treatment for the various types of such cases, to call attention to the difficulties of avoiding such accident under the many stresses of abdominal work, and to arouse interest in the serious study of the problem of prevention." Complete and detailed analyses of all case records are tabulated and the problem of diagnosis and treatment is discussed.

The chapter concerned with measures of prevention is in itself a comprehensive treatise upon the many devices employed in the interest of safety from the earliest sponge count down to fiberglas thread and "rayable" gauze.

It has been said that medico-legal records confirm the belief that a good deal more trouble is caused by leaving too much within the abdomen than by taking too much out. The various legal aspects of this problem are clearly defined by the co-authur and a table of court actions in foreign body cases is presented.

There is an exhaustive bibliography compiled with great care and effort. When ultimately a solution is found to the foreign body problem I earnestly believe that it will be in tribute to this fine book.

E. F. L.

Physiology of Micturition. Experimental and Clinical Studies with Suggestions as to Diagnosis and Treatment. By ORTHELLO R. LANGWORTHY, LAWRENCE C. KOLB and LLOYD G. LEWIS. 232 pp. Illus. $3.50. *The Williams & Wilkins Co., Baltimore, 1940.*

This interesting monograph contains a very complete description of the mechanism and control of bladder function. The book is divided into six major sections which are comprised of chapters dealing with the anatomy, pharmacology, physiology, peripheral nerves and spinal cord (as involved in bladder control), the brain in relation to micturition and clinical diagnosis. These chapters include much information of value to both clinicians and experimentalists.

The authors deal chiefly with the bladder of man and that of the cat. Pertinent literature is well listed and summarized. It is difficult to exclude physiological considerations from a discussion of the anatomy of the bladder. Both anatomy and physiology must be considered in interpreting clinical observations. There is consequently some repetition of material in the various subdivisions of the book. Each chapter is a complete essay in itself. The information collected therein and the authors' interpretations are very clearly presented. Brief summaries at the ends of the chapters are helpful.

The most unique portions of the monograph are those dealing with the role of various levels of the central nervous system in controlling bladder activity and the chapters in which are given an analysis and an explanation of bladder abnormalities occurring frequently in man.

C. McC. B.

The Relativity of Reality. By RENÉ LAFORGUE. Translated by ANNE JOUARD. 92 pp. $2.50. Nervous and Mental Disease Monographs [No. 66], New York, 1940.

After a preliminary chapter on anxiety and another on the conflicts in the affective development of man, Dr. Laforgue launches into a discussion of what he describes as the relativity of reality. His viewpoint is summarized in the following two sentences which appear toward the end of the third chapter: "The conception of reality, as we see it, is therefore in a large measure a function of development of the libido of the ego, both individual and collective. It would seem that this development must of necessity go through oral, anal and genital stages before arriving at the conception of reality as it appears to us."

The above quotation illustrates the author's psychoanalytic slant. He frequently writes in a vivid way concerning the psychological and emotional stages in the growth of the individual from self-centered childhood to full maturity. The presentation, however, seems somewhat cramped by his adherence to a set of classifications which violates one's sense of life. In his division of the personality into the super-ego, the ego, and the id, he follows orthodox Freudian tradition and almost goes the length of attributing an independent will and purpose to each of these functions. In his account of childhood and adolescence, moreover, he not only re-emphasizes the analytic "Oedipus situation" but adds what he describes as an earlier "negative" Oedipus relationship with attachment to the parent of the same sex.

His own division of individuals into anal and genital intellectual types is given with life-like illustrations and one can only regret that his own work does not have more of those wholly admirable "genital" traits including freedom from excessive classification and respect for what he himself describes as "sound common sense."

H. F.

Rheumatic Fever. By MAY G. WILSON. 595 pp. $4.50. *The Commonwealth Fund. New York, 1940.*

This book presents a large amount of material on the natural history of rheumatic fever as observed by the author during the past twenty-five years. She has made extensive studies on the epidemiology, etiology, manifestations, course, diagnosis, prognosis and treatment of the disease, most of which she has published previously in separate articles. The observations were made primarily upon children, some of whom were followed into the third decade of life.

There is much of interest scattered through the large volume. Bacteriological and immunological investigations do not lead the author to believe that there is any specific etiological relationship between rheumatic fever and either respiratory infections or scarlet fever or the beta hemolytic streptococcus. The section on radioscopic examination describes the author's method of determining the angle of clearance of the left ventricle in order to ascertain whether enlargement is present which may not be visible in the ordinary teleoroentgenogram.

References to the investigations of others working on the problem of rheumatic fever are purposely brief, and the author states she has no intention of making a "comprehensive critical review" of the subject. Nevertheless, a good many pages are devoted to scanty summaries of the literature, with fairly voluminous bibliographies appended to every chapter or group of chapters. It seems unfortunate that many of these references are so incomplete that they fail to develop the argument satisfactorily, and the author does not evaluate the material critically in an effort to resolve apparently conflicting results. Finally, references are not numbered, so that when the text refers to work done by "various investigators" without giving the names of authors, there is no way for the reader to find the original article.

Eighty pages are devoted to charts of 647 case histories reduced so completely to symbols that it takes much time and devotion to unravel them. Material has been added on the nomenclature and classification of heart disease, as well as numerous tables of standards for the various ages of childhood.

Somehow, the book does not seem entirely suited to any class of reader. It is not detailed or discursive enough for the specialist in rheumatic fever and rheumatic heart disease; it is too diffuse for the general practitioner and not specific enough for the student.

C. B. T.

Introduction to Medical Biometry and Statistics. By RAYMOND PEARL. 3rd ed. 537 pp. Illus. $7.00. *W. B. Saunders Company, Philadelphia and London, 1940.*

The third edition of Dr. Pearl's text on Medical Biometry and Statistics appeared fortunately before his death on November 17, 1940. The first two editions of his book undoubtedly had more to do with the advancement of this field than any other one text. Ten years had elapsed since the publication of the second edition during which time many changes had been seen in the theory and practice of medical statistics. The changes included in the new edition are: (1) the omission of the International List of Causes of Death, (2) a discussion of the integration of records using the Eastern Health District records as an example, (3) the Reed-Merrell method for computing an abridged life table, (4) a complete new chapter on variation, and (5) many new tables in the appendix to assist in routine computation.

E. L. C.

The Neuroses in War. By several authors. Edited by EMANUEL MILLER. 250 pp. $2.50. *The Macmillan Company, New York, 1940.*

Under the editorship of Emanuel Miller a group of ten psychiatrists has collaborated in the writing of a dozen or so articles concerned with various aspects of war psychiatry. Most of the writers saw service in the first world war as psychiatrists or neurological consultants to the British Army. The majority of them are connected with the Tavistock Clinic in London and their outlook is psychoanalytic.

Since the book was written primarily for the guidance of physicians in positions of responsibility in the present war, attention has been given to civilian problems as well as to those not directly related to army service. Written in large part before the severe air raids over London had begun, the chapter on civilian morale is necessarily of a more or less theoretical nature and, as a matter of fact, much of the rest of the book is a summary of experiences growing out of the trench warfare of twenty-five years ago, which may or may not have a particularly direct bearing on the problems that are being confronted today.

Although in reading through this volume one has the impression that careful arrangement of the material with clear emphasis of the leading concepts has been sacrificed to what may well have been the pressing haste in getting it published, there are many valuable hints concerning the diagnosis and treatment especially of the protean forms of hysteria and anxiety as they are met in a military setting. "Shell shock" and the notorious label "D.A.H.", for example, are critically evaluated and most of the authors stress the personal emotional factors as primarily responsible for both of these conditions. Although prompt and forceful treatment including especially direct persuasian and hypnosis, is recommended, the authors show a healthy respect for the underlying personality make-up of the men involved and one of them even goes so far as to state that ten per cent of the patients who landed in special psychiatric hospitals actually should have been candidates for admission to a mental institution even before the war started. The case illustrations are often somewhat fragmentary but the book is pre-eminently practical and it is certainly well worth the attention of any physician likely to see military service in the present war.

H. F.

Practice of Medicine. By JONATHAN CAMPBELL MEAKINS. 3rd ed. 1430 pp. Illus. $10.00. *C. V. Mosby Company, St. Louis, 1940.*

The third edition of this excellent book is now available. Its scope is very comprehensive, and the results are about as consistently good as one could wish in such circumstances. Since a number of infectious diseases not indigenous to North America are included, it might be wise to include among the Septicemias that of Suipestifer infection. An error in the calculation of the dose of digitalis reported in a previous edition by this reviewer has been corrected.

J. T. K.